Chapter 5
Classification of Drugs, Nutraceuticals, Functional Food, and Cosmeceuticals; Proteins, Peptides, and Enzymes as Drugs

Abstract A crude drug is a naturally occurring unrefined substance consisting of whole plant or herb, any part of it, exudate or extract of it. Crude drugs of different sources are arranged (i) in alphabetical order of their Latin (e.g., European pharmacopoeia) and English (e.g., USP and BPC) names, common names, or sometimes local language names (e.g., Acacia, Benzoin, Cinchona, Dill, Ergot, Fennel); (ii) according to structural characteristics as organized (e.g., part or organ of the plant and animal such as leaves, stems, roots, rhizome, barks, flowers, seeds, hair, fibers) and unorganized drugs (e.g., acellular products of plant and animal such as gum, latex, juice, oil); (iii) following the principles of natural relationship and evolutionary development of plants or animals taxa in Phyla, Orders, Families, Genera, Species, Sub-species, etc.; (iv) according to their pharmacological action or therapeutic uses (e.g., bulk purgatives, emollient purgatives; digitalis, squill, and strophanthus cardiotonics), (v) on the basis of the chemical nature of important constituent or their biosynthetic pathways (e.g., alkaloids, glycosides), (vi) on the chemical similarity of a taxon or certain classes of plants (e.g., tropane alkaloids as a chemotaxonomic marker of Solanaceae members; berberine alkaloid in Berberis and Argemone; rutin in Rutaceae members; ranunculaceous alkaloids in Ranunculaceae) in (i) alphabetic, (ii) morphological, (iii) taxonomical, and (iv) pharmacological or therapeutic (v) in chemical (vi) in chemotaxonomic systems of classifications. The classification of allopathic drugs is based on the clinical usage may be grouped into non-prescription drugs or over-the-counter drugs and prescription drugs. The anatomical therapeutic chemical (ATC) classification of modern drugs is a more elaborate one that categorizes drugs into 14 main classes according to the organ or biological system on which they act as well as their therapeutic, pharmacological, and chemical properties. On the basis of properties and uses, allopathic drugs are also classified as antibiotics, antacids, antigas medicines, wormicides, steroid medicines, medicines for the external uses, antiallergens and antihistamines, antihypertensive, antidiabetic, antidiarrheal medicines, laxatives, medicines for anticold and cough, antiepileptic, antispasmodic, antipyretics, analgesics, antivomiting, antiulcer, hematinic, tranquillizers, medicines for giddiness, enzymes, vitamins, mineral compounds, amino acids, etc. Nutraceuticals are medicinal foods, nutritional supplements, dietary supplements, or

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food components made from herbal or botanical raw materials that can deliver health benefits beyond basic nutrition, modulate immunity, and/or prevent and cure specific diseases and increase life expectancy. They cover a wide spectrum of substances ranging from natural diets, herbal products, biofortified crops, genetically modified and processed food products. Nutraceuticals are classified as traditional or natural nutraceuticals (e.g., nutrients, herbals, phytochemicals, probiotic microorganisms, nutraceutical enzymes) and non-traditional or artificial nutraceuticals (e.g., fortified and recombinant nutraceuticals). Cosmeceutical is a hybrid combination of cosmetics and pharmaceuticals containing biologically active ingredients to add medical or drug-like benefits (e.g., cream, lotion, ointment and similar other substances containing botanical and marine extracts like vitamins, peptides). These products are intended for the improvement of health and beauty of the skin and hair. They contain a wide spectrum of biologically active ingredient of natural origin including moisturizer, vitamin, sun protector, skin whitener, free radical scavenger, etc. Cosmeceuticals are classified on the basis of (a) use: (i) skin cosmeceutical products, (ii) hair cosmeceutical products, and (iii) others; (b) active ingredient content and function as (i) retinoids, (ii) sunscreens, (iii) moisturizers, (v) depigmenting agents, (vi) exfoliants, (vii) antioxidants, (viii) proteins/peptides, and (ix) growth factors.

Keywords Classes of drugs · Nutraceuticals · Cosmeceuticals · Biofortified foods

5.1 Classification of Crude Drugs

Higher plants, microbes, animals, and minerals are the main natural sources of crude drugs. Enzymes and antibiotics used in modern medicine are also obtained from natural biological sources. Classification is a means of the systematic arrangement of large varieties or quantities of things into smaller groups on the basis of some similar characters present in them. A method of classification should be simple, easy to use, and free from confusion and ambiguities. In order to conveniently study crude drugs of different origin, it is necessary to classify them into some smaller groups by using certain criteria, i.e., according to morphological, taxonomical, chemical, and pharmacological characters. Morphological classification is more helpful to identify and detect adulteration; for studying evolutionary developments, the drugs are classified according to taxonomical classification, the activity of a drug is due to its chemical constituents, and therefore, the drugs are divided according to the presence of chemical components and pharmacological classification of drugs is more relevant to study therapeutic utility of the drugs. However, each of these systems has its own merits and demerits.

5.1.1 Alphabetical Classification

Alphabetical classification is the simplest way of classification of any disconnected items. Crude drugs are arranged in alphabetical order of their Latin and English names (common names) or sometimes local language names (vernacular names). Some of the examples are as follows: Acacia, Benzoin, Cinchona, Dill, Ergot, Fennel, Gentian, Hyoscyamus, Ipecacuanha, Jalap, Kurchi, Liquorice, Mints, Nux-vomica, Opium, Podophyllum, Quassia, Rauwolfia, Senna, Vasaka, Wool fat, Yellow bees wax, Zeodary. In European pharmacopoeia, these are arranged according to their names in Latin, where in USP and BPC, these are arranged in English.

Some of the pharmacopoeias, dictionaries, and reference books, which classify crude drugs according to this system, are as follows:

i. Indian pharmacopoeia;
ii. British pharmacopoeia;
iii. British Herbal pharmacopoeia;
iv. US pharmacopoeia and National Formulary;
v. British Pharmaceutical Codex;
vi. European pharmacopoeia;
vii. Bangladesh pharmacopoeia; and
viii. International pharmacopoeia.

In addition, a number of the more enlightened nations have pharmacopoeias, so there are the German pharmacopoeia, the Swiss, the Japanese, etc. The pharmacopoeia (literally, 'drug-making') is a book which defines and standardizes certain drugs and their preparations. It is a reference work for pharmaceutical drug specifications. Its aim is to establish definiteness for a selected number of those in extensive use by physicians. The pharmacopoeia's drugs and preparations are considered as official and protected by one or more National Acts related to Food and Drugs Policies. The official preparations are, therefore, the ones that are standardized; hence, they are the preparations that can be obtained of uniform strength throughout the country, and they are, for the most part, the forms in which remedies can be readily supplied by the pharmacist. Hence, the official preparations are the forms to be preferred by the physician.

The International pharmacopoeia (Ph. Int.) is published by the WHO with the aim to achieve a wide global harmonization of quality specifications for selected pharmaceutical products, excipients, and dosage forms. The activities related to Int. Ph. are an essential element in overall quality control and assurance of pharmaceuticals contributing to the safety and efficacy of medicines. The work of the International pharmacopoeia is carried out in collaboration with members of the WHO Expert Advisory Panel on the International pharmacopoeia and Pharmaceutical Preparations and with other specialists.

Merits

i. It is easy and quick to use;
ii. There is no repetition of entries and is devoid of confusion; and
iii. In this system location, tracing and addition of drug entries are easy.

Demerits

i. There is no relationship between previous and successive drug entries.

5.1.2 Morphological Classification

Under morphological classification, the drugs are arranged according to the part or organ of the plant and animal used such as leaves, stems, roots, rhizome, barks, flowers, seeds, hair, and fibers (organized drugs) and plant product such as gum, latex, juice, and oil (unorganized drugs). The organized drugs are obtained from the direct parts of the plants or animals and containing cellular tissues, whereas the unorganized drugs are prepared from plants or animals by some intermediate physical processes such as incision, drying, or extraction with a solvent and do not contain any cellular tissues.

According to this system, crude drugs are broadly divided into the following two main groups on the basis of their apparent morphological forms of occurrence and structural organization of the plant or animal parts and their natural products:

i. **Organized drugs**: The drugs obtained from the direct parts of the plants and animals and containing cellular tissues are known as organized drugs, e.g., rhizomes, barks, leaves, fruits, entire plants, hair, and fibers.
ii. **Unorganized drugs**: The drugs which are prepared from plants or animals by some intermediate physical processes such as incision, drying, or extraction with a solvent and not containing any cellular plant or animal tissues are called as unorganized drugs. Aloe juice, opium latex, agar, gambir, gelatin, tragacanth, benzoin, honey, beeswax, lemon grass oil, etc., are examples of unorganized drugs.

Differences between organized and unorganized drugs are shown below in tabular form (Table 5.1).

The organized crude plant drugs are further divided into the following two groups according to the position of the plant organs that constitute the crude drugs:

i. **Drugs from over ground organs**: These include all drugs that are derived from the overground or aerial parts or organs of plants.
ii. **Drugs from underground organs**: These include all drugs that are derived from underground or subterranean parts or organs of plants.

Table 5.1 Differences between organized and unorganized drugs

Organized drugs	Unorganized drugs
(i) These may be of plant or animal origin	(i) These may be of plant, animal, or mineral origin
(ii) These are direct part of plant or animal	(ii) These are the product of plant, animal, or mineral
(iii) These have cellular structure	(iii) These do not have well-defined cellular structure
(iv) Generally identified by morphological character	(iv) Generally identified by organoleptic properties
(v) Examples: digitalis leaf, cinchona bark, ephedra stem, etc.	(v) Examples: Agar, gelatin, honey, etc.

The crude drugs of the over ground organs are again divided into herb, leaf, flower, fruit, seed, bark, and wood drugs and those of the underground organs into root, rhizome, bulb, and corm drugs on the basis of their morphological identity. The unorganized crude drugs are also similarly divided into smaller groups on the basis of the nature of the natural product, such as juices, lattices, extracts, gums, resins and balsams, fats, oils, and waxes.

Classification of drugs on the basis of morphological characters with example is given in Table 5.2.

Merits

i. Morphological classification is more helpful to identify and detect adulteration.
ii. This system of classification is more convenient for practical study, especially when the chemical nature of the drug is not clearly understood.

Demerits

i. The main drawback of morphological classification is that there is no correlation of chemical constituents with the therapeutic actions.
ii. Repetition of drugs or plants occurs.

5.1.3 Taxonomical Classification

Taxonomical classification is purely a botanical classification and is based on the principles of natural relationship and evolutionary developments. The drugs are classified according to plants or animals from which they are obtained into Phyla, Orders, Families, Genera, Species, Sub-species, etc. (Table 5.3).

As all the entire plants are not used as drugs, part of the plant is used as a drug, for example, cinnamon bark, and thus, it is of no significance from an identification point of view to put plants in a taxonomic order. Table 5.4 gives the account of

Table 5.2 Classification of drugs on the basis of morphological characters with example

Classification of drugs	Drug examples
1. Organized drugs	
(i) Wood	Quassia, Sandal wood, Red Sandal wood
(ii) Leaves	Digitalis, Eucalyptus, Gurniar, Pudina, Senna, Spearmint. Squill, Tulsi, Vasaka, Coca, Buchu, Hamamelis, Hyoscyamus, Belladonna, Tea
(iii) Barks	Arjuna, Ashoka, Cascara, Cassia, Cinchona, Cinnamon. Kurchi, Quillaia, Wild Cherry
(iv) Flowering parts	Clove, Pyrethrum, Saffron, Santonica, Chamomile, Artemisia
(v) Fruits	Amla, Anise, Bahera, Bitter orange peel, Capsicum, Caraway, Cardamom, Cassia, Colocynth. Coriander, Cumin, Dill, Fennel, Gokhru, Hirda, Lemon peel, Psoralea, Senna pod, Star anise, Tamarind, Vidang, Bael
(vi) Seeds	Bitter almond, Black mustard, White mustard, Cardamom, Colchicum, Linseed, Neem, Nutmeg, Nux vomica, Physostigma, Psyllium, Strophanthus, Isabgol, Castor
(vii) Roots, rhizomes and bulb	Aconite, Ashwagandha, Calamus, Calumbs, Colchicum conn, Dioscorea, Calanga, Garlic, Gentian, Ginger, Ginseng, Glycyrrhiza, Podophyllum, Ipecac, Iponnea, Jalap, Jatamansi, Male fern, Picrorhiza, Piplam, Rauwolfia
(viii) Plants and herbs	Rhubarb, Saussurea, Senega, Shatavari, Turmeric, Valerian, Squill, Serpentary, Indian Podophyllum, Krameria, Derris, Indian Valerian, Andrographis, Bacopa, Banafsha, Belladonna, Cannabis, Centella, Chirata, Chondrus, Datura, Ephedra, Ergot, Hyoscyamus. Kalmegh, Lobelia, Punarnava, Shankhpushpi, Stramonium, Vinca, Yeast, Cantharides
(ix) Hair and fiber	Cotton. Hemp, Jute, Silk, Flax
2. Unorganized drugs	
(i) Dried latex	Opium, Papain, Gutta-percha
(ii) Dried juice	Aloe, Kino, Red gum
(iii) Dried extracts	Agar, Alginate, Black Catechu, Pale Catechu, Pectin, Gelatin, Curare
(iv) Gums	Acacia, Guar gum, Indian gum, Sterculia, Tragacanth, Ghatti gum
(v) Resins	Asafoetida, Benzoin, Colophony, Copaiba, Guaiacum, Guggal, Mastic, Myrrh, Peru Balsam, Sandarac, Storax, Tolu balsam, Tar, Coal tar
(vi) Fixed oils and fats	Arachis, Castor, Chaulmoogra, Coconut, Cottonseed, Linseed, Olive, Sesame, Almond, Theobroma, Lard, Cod liver, Halibut liver, Kokum butter
(vii) Waxes	Beeswax, Spermaceti, Carnauba wax
(viii) Volatile oil	Turpentine, Anise. Coriander. Peppermint, Rosemary, Sandalwood, Cinnamon, Lemon, Caraway, Dill, Clove, Eucalyptus, Nutmeg, Camphor

(continued)

Table 5.2 (continued)

Classification of drugs	Drug examples
(ix) Animal products	Beeswax, Cantharides, Cod-liver oil, Gelatin, Halibut-liver oil, Honey, Shark-liver oil, Shellac, Spermaceti wax, Wool Fat, Musk, Mylabris, Lactose
(x) Fossil organisms and minerals	Bentonite, Kaolin, Kiesselguhr, Talc

Table 5.3 Drugs are classified into phyla, orders, families, genera, species, sub-species

Phylum	Order	Family	Genus	Species
Gymnosperms	Gnetales	Ephedraceae	*Ephedra*	*E. sinica*
Angiosperm: Dicotyledons	Rhoedales Rhanales	Papaveraceae Rhamnaceae	*Papaver* *Zizyphus*	*P. somniferum* *Z. mauritiana*
Angiosperm: Monocotyledons	Glumiflorae Liliflore	Poaceae Liliaceae	*Cynodon* *Allium*	*C. dactylon* *A. sativum*

main characters of various taxa that contribute crude drugs, while Table 5.5 gives the taxonomical classification of some drugs.

Merits

Taxonomical classification allows for precise and ordered arrangement of drugs and accommodates any drug without ambiguity, and it is helpful for studying evolutionary development.

Demerits

This system does not correlate in between the chemical constituents and biological activity of the drugs. This system of classification is criticized for its failure to recognize the organized and unorganized nature of crude drugs and chemical nature of active constituents and therapeutic significance of crude drugs.

5.1.4 Pharmacological Classification

This pharmacological or therapeutic classification involves the grouping of drugs according to their pharmacological action of active constituents or their therapeutic uses, regardless of their morphology, taxonomical status, or chemical relationships. The drugs differing in mechanism of action but having same pharmacological effects are also grouped together, e.g., bulk purgatives, irritant purgatives, emollient purgatives. This classification is more relevant and is mostly followed method. Thus, drugs like digitalis, squill, and strophanthus having cardiotonic action are grouped together irrespective of their parts used, phylogenetic relationship, and the

Table 5.4 Main characters of various taxons that contribute crude drugs

Plant kingdom or *Plantae*	Characteristics
Non-vascular plants	
Thallophyta	(i) Algae and fungi are consider together (ii) They differ in mode of nutrition (iii) Algae exhibit autotrophic and fungi exhibit heterotrophic nutrition. Example: agar of Rhodophyta; sclerotium of *Claviceps purpurea* (Ascomycota)
Bryophyta	(i) Bryophytes are non-vascular embryophytes (land plants) (ii) Plants do not contain vascular tissues; some have specialized tissues for the transport of water (hydroids) (iii) Life cycles are dominated by the gametophyte stage (iv) Includes Hepaticea (Liverworts—Riccia, Marchantia), Anthocerotae (Anthoceros), and Musci (Mosses); example: *Sphagnum, Polytrichum*
Vascular plants	
Pteridophyta	(i) This group of plant derives its name from the fern, *Pteris,* which also represents salient features of the group (Pterido-*pteris*, Phyton-plant) (ii) They occur is humid and tropical climates and usually ground on soil, rocks, in ponds, etc. (iii) These plants are also raised in pots as ornamentals Example: Male fern
Gymnosperm	(i) The gymnosperm (gymnos-naked and sperma-seed, i.e., plant with a naked seeds) is comparatively more ancient than the angiosperm in evolutionary terms (ii) The living gymnosperms are widely distributed in the cold climates (iii) The plant body is sporophyte and differentiated into roots, stem, and leaves Example: Ephedra, Colophony
Angiosperm	(i) The term angiosperm means enclosed seed because the ovules or potential seed is enclosed within a hallow ovary (ii) The angiosperms constitute the most dominant and ubiquitous vascular plants of present-day flora (iii) Dicots and monocots are its subdivisions
Angiosperm	**Monocotyledons**—They have one cotyledon in the seed. Example: Vanilla, Colchicum
	Dicotyledons—They have two cotyledons in the seed. Example: Coriander, Capsicum

Angiosperms Phylum	Order	Family	Drugs
Monocotyledons	Liliflorae	Liliaceae Dioscoreaceae	Scilla Colchicum Asparagus Dioscorea

(continued)

Table 5.4 (continued)

Angiosperms Phylum	Order	Family	Drugs
Dicotyledons	Microspermae Papaverales Rosales Rutales Rhamnales Malvaies Umbelliflorae Gentianales Tubiflorae	Orchidaceae Papaveraceae Rosaceae Leguminosae Rutaceae Rhamnaceae Malvaceae Apiaceae Loganiaceae Gentianaceae Apocyanaceae Convolvulaceae Lamiaceae	Vanilla Opium Almond Quillaia Rose oil Balsam of Tolu Glycyrrhiza Senna Bael, Lemon Orange peel Cascara Bark Sida
	Plantaginales Dipsacates Campanulales	Solanaceae Scrophulariaceae Plantaginaceae Valerinanceae Lobeliaceae Asteraceae	Coriander Caraway Dill, Fennel Nux-vomica Chirata Rauwolfia Strophanthus Shankhpushpi (Convolvulus pluricaulis) Mentha Ocinuim Belladonna Solanaceae Capsicum Datura Hyoscyamus Figworts, mulleins Digitalis Plantago Valerian Lobelia Artemisia Costus or Kuth
Gymnosperms	Genetales Coniferae	Ephedraceae Finacea	Ephedra Colophony
Bryophyta and Pteridophyta (Liverworts, Mosses and Ferns)	Marchantiales Polytrichales Filicales	Marchantiaceae Polytrichaceae Polypodiaceae	*Marchantia* *Polytrichum* Male fern
Thallophyta (Bacteria, Fungi, Lichens) Rhodophyta	Gelidiales	Gelidiaceae	Agar

Table 5.5 Taxonomical classification of some crude drugs

Phyllum	Order	Family	Drugs
Thallophyta (Algae, Fungi, Lichens)	Gelidiales Hypocreales Lecanorales	Gelidiaceae Clavicipitaceae Parmeliaceae	Agar ergot *Usnea* spp.
Bryo- and Pteridophyta (Liverhorts, Mosses and Ferns)	Marchantiales Sphagnales Dryopteridales	Marchantiaceae Sphagnaceae Dryopteridaceae	Marchantia Sphagnum Dryopteris/male fern
Gymnosperms	Genetales Coniferae	Ephedraceae Pinaceae	Ephedra Colophony
Angiosperms (Monocotyledons)	Liliflorae Microspermae	Liliaceae Dioscoreaceae Orchidaceae	Colchicum Dioscorea Vanilla
Angiosperms (Dicotyledons)	Rosales	Fabaceae	*Glycyrrhiza glabra*, *Astragalus gummifer*, Myroxylon balsamum
	Tubiflorae	Solanaceae	Atropabelladonna, Hyoscyamusniger, Daturastramonium

nature of phytoconstituents they contain. Table 5.6 gives an outline of pharmacological classification of drugs.

Merits

This system of classification can be used for suggesting substitutes of drugs if they are not available at a particular place or time.

Demerits

Drugs having different action on the body get classified separately in more than one group that causes ambiguity and confusion. Cinchona is an antimalarial drug because of the presence of quinine, but can be put under the group of drug affecting heart because of antiarrhythmic action of quinidine.

But purely pharmacological classification for herbal materials is difficult because of the numerous conditions for which any one traditional method may be employed. Based on the pharmacological response, the herbal medicines can be grouped under the following categories. Some of the major pharmacological groupings include herbal medicines which act on the nervous systems, the heart and blood vessel, the lungs, the gastrointestinal tract, the kidneys, the skin, and mucus membranes. Other categories include hormones (steroids), vitamins, and chemotherapeutic medicines used for the treatments of infections and malignant diseases. All these may also be classified as (a) systemic (function through the organized systems) and (b) non-systemic (localized action) medicines.

Table 5.6 Classification of drugs based on pharmacological action

Pharmacological or therapeutic classes	Name of drugs
Malignant growth inhibitors	
1. Anticancer (suppresses malignant growth)	1. Vinca, Podophyllum, Taxus, Camptotheca
2. Antiinflammatory (suppresses inflammation)	2. Colchicum corm and seed, turmeric
Drugs acting on gastrointestinal tract	
3. Bitter principles	3. Gentian, Quassia, Cinchona, Nux-vomica, Gentian, Picrorhiza, Chirata, Kalmegh
4. Carminatives (relieves flatulence or excess gas in the stomach or bowels)	4. Dill, Mentha, Gentian, Cinnamonbark, Cardamom seed
5. Emetics (a drug that causes vomiting)	5. Ipecacuanha
6. Antiamoebic (suppresses amoebic infection)	6. Ipecac root, Kurchi bark
7. Bulk laxatives (looses bowels and relieves constipation)	7. Agar, Ispaghula, Banana
8. Purgatives (evacuates bowels)	8. Senna, Castor oil, Cascara bark, Rhubarb, Aloe, Plantago seed husk
9. Peptic ulcer	9. Derivatives of Glycyrrhetinic acid (Liquorice and Raw banana)
10. Antiasthmatic (corrects bronchial disorder)	10. Ephedra, Lobelia, Vasaka, Tylophora
11. Anthelminthic (kills intestinal parasitic worms)	11. Male fern, Quassia wood, Artemisia, Vidang, Chenopodium oil
Antispasmodic (*cures convulsion or tonus of pain muscle*)	
12. Smooth Muscle Relaxants	12. Datura, Hyoscyamus, Belladonna; Opium, Datura, Hyoscyamus
13. Skeletal Muscle Relaxants	13. Curare
14. Astringent (styptic, stop bleeding)	14. Catechu, Tannic acid, Myrrh, Myrobalan, Ashoka bark
15. Analgesic (relieves pain, reduces temperature)	15. Opium, poppy, Cannabis
16. Flavors	16. Nutmeg fruit, Clove, Umbelliferous fruits, Peppermint, Saffron, Asafoetida, Oleo-gum resin. Mint, Tulsi, Ginger, Vanilla
Drugs acting on respiratory system	
17. Expectorant (relieves cough from the lung)	17. Senna, Rhubarb, Benzoin, Balsam of Tolu, Glycyrrhiza, Vasaka, Tulsi
18. Antiexpectorant	18. Stramonium leaves (Atropine)
19. Antitussives (prevents or relieves cough)	19. Opium (Codeine, Noscapine)
20. Brochodilator (dilates bronchi and bronchioles)	20. Ephedra, Tea (Theophylline)

(continued)

Table 5.6 (continued)

Pharmacological or therapeutic classes	Name of drugs
Drugs acting on cardiovascular systems	
21. Cardiotonic	21. Digitalis, Squill, Strophanthus
22. Cardiac depressants	22. Cinchona (quinidine), Veratrum
23. Vaso-constrictors (causes constriction of blood vessels)	23. Ergot (ergotamine), Ephedra
24. Tranquilizers (reduce anxiety), Antihypertensives (reduce blood pressure)	24. Rauwolfia Roots, Cocaine, Cannabis
Drugs acting on autonomic nervous systems	
25. Adrenergics	25. Ephedra
26. Cholinergics (related to choline and liver function)	26. Physostigma, Pilocarpus
27. Anticholinergics	27. Belladonna, Datura
Drugs acting on CNS	
28. CNS stimulants	28. Coffee (caffeine)
29. Analeptics	29. Nux-vomica, Lobelia, Camphor
30. CNS depressants	30. Hyoscyamus, Belladonna, opium
31. Hallucinogenics (cause error in perception)	31. Cannabis, Poppy latex
32. Antirheumatics (relieve the pain of rheumatism)	32. Aconite, Colchicum, Guggul

(a) **Systemic**

(i) Medicines act on the automatic nervous system;
(ii) Medicines act on the central nervous system;
(iii) Medicines act on the heart muscle;
(iv) Medicines act on the blood vessels;
(v) Promotion of diuresis (in case renal flow);
(vi) Action on the respiratory system;
(vii) Action on the gastrointestinal tract;
(viii) Action on the liver; and
(ix) Action on the uterus.

(b) **Non-systemic**

(i) Action on the skin and mucous membranes;
(ii) Action on sugar metabolism;
(iii) Steroids and antiinflammatory drugs;
(iv) Treatment of malignant diseases;
(v) Treatment of infections;
(vi) Treatment of allergies; and
(vii) Vitamins.

Drugs are either (i) pure chemicals, such as sodium bicarbonate or potassium iodide; (ii) mixed mineral products, such as petroleum oil, vaseline, or ichthyol; or (iii) certain animal or plant parts or products. Of animal nature or origin are musk, cantharides, adrenaline, lard, honey; of plant nature or origin are herbs, barks, roots, leaves, fruits, seeds, resins, alkaloids, etc.

5.1.5 Chemical Classification

The biological activity of a drug is due to the presence of certain chemical constituents in it. Plants and animals synthesize chemical compounds such as fats, carbohydrates, proteins, volatile oils, alkaloids, and resins, and some of these are pharmacologically active constituents. A single active constituent may be isolated from the crude drug and used as a medicinal agent. More than 75 pure compounds derived from higher plants find their place in modern medicine. For example, the important traditional active drug principles are codeine, atropine, ephedrine, hyoscyamine, digoxin, hyoscine, digitoxin, pilocarpine, theobromine, theophylline, quinidine, quinine, emetine, caffeine, papaverine, and colchicine. These active constituents are differentiated from the inert compounds like starch, cellulose, lignin, and cutin.

According to this system, the crude drugs are divided into different groups on the basis of the chemical nature of important constituent. Since the pharmacological activity and therapeutic significance of crude drugs are based on the nature of their chemical constituents, the chemical classification of drugs is dependent upon the grouping of drugs with identical constituents. An out of this classification is as follows (Table 5.7):

Merits
It is a popular approach for phytochemical studies. The chemical classification of crude drugs seems to be the preferred method of study, since biological activities of crude drugs (therapeutic and pharmacological activities) are based on the chemical constituents of crude drugs.

Demerits
Ambiguities arise when particular drugs possess a number of compounds belonging to different groups of compounds, i.e., drugs which contain two or more types of chemical constituents cannot get appropriate placement by this system.

Table 5.7 Classification of drugs on the basis of chemical nature

	Chemical constituents	Drugs
1.	**Carbohydrates** Carbohydrates are polyhydroxy aldehydes or ketones containing an unbroken chain of carbon atoms (i) Gum (ii) Mucilages (iii) Others	(i) Acacia, Tragacanth, Guargum, Sterculia (ii) Plantago seed (iii) Starch. Honey, Agar, Pectin; Pectin. Bael, Cotton
2.	**Glycosides** Glycosides are compounds which upon hydrolysis give rise to one or more sugars (glycone) and non-sugar (aglycone) (i) Anthraquinoneglycosides (ii) Saponins glycosides (iii) Cyanophore glycosides (iv) Isothiocyanate glycosides (v) Cardiac glycosides (Steroidal) (vi) Bitter glycosides	(i) Aloe, Cascara, Rhubarb, Senna (ii) Quillaia, Arjuna, Glycyrrhiza, Dioscorea (iii) Wild Cherry bark (iv) Mustard (v) Digitalis. Strophanthus, Squill, Scilia (vi) Gentian. Calumba. Quassia Chirata, Picrorhiza, Kalmegh
3.	**Tannins** Tannins are complex organic, non-nitrogenous derivatives of polyhydroxy benzoic acids	Pale Catechu, Black Catechu, Ashoka bark, Galls, Myrobalan, Behera, Amla
4.	**Volatile oils** Monoterpenes and sesquiterpenes obtained from plants	Cinnamon, Nutmeg, Fennel, Dill, Caraway, Coriander, Cardamom, Orange peel, Mint, Clove, Ginger, Valerian, Saffron, Banafsha, Tulsi, Anise, Lemongrass, Jatamansi
5.	**Lipids** (i) Fixed oils (ii) Fats (iii) Waxes	(i) Castor, Olive, Peanut, Almond, Shark liver oil (ii) Cottonseed, Theobroma (iii) Lanolin, Theobroma, Lanolin, Beeswax, Spermaceti
6.	**Resins and Resin combinations** Complex mixture of compounds like resinols, resin acids, resinotannols, resenes (i) Resins (ii) Glycosidal resins (iii) Oleo resins (iv) Oleo gum resin (v) Balsam	(i) Colophony (ii) Podophyllum, Jalap, Kaladana (iii) Capsicum, Ginger (iv) Asafbetida, Guggul (v) Storax, Tolu balsam, Peru balsam, Benzoin
7.	**Alkaloids** Nitrogenous heterocyclic compounds of plant origin (i) Pyridine and Piperidine (ii) Tropane (iii) Quinoline (iv) Isoquinoline	(i) Lobelia,Nicotiana, Areca nut, Anabasis,Sedum (ii) Coca, Belladonna, Datura, Hyoscyamus, Stramonium, Henbane (iii) Cinchona, Dictamnus (iv) Opium, Ipecacuhuna, Amaryllis, Lycoris

(continued)

Table 5.7 (continued)

	Chemical constituents	Drugs
	(v) Indole (vi) Amines (e.g. vincamine-monoterpenoid indole alkaloid) (vii) Purine (viii) Steroidal (ix) Diterpene (x) Phenanthrene	(v) Ergot, Nux vomica, Rauwolfla (vi) Catharanthus, Physostigma, Ephedra (vii) Tea, Coffee (viii) Holarrhena, Solanum, Veratrums (ix) Aconitum (x) Opium
8.	**Proteins and enzymes**	Gelatin, Yeast, Ficin, Papain, Casein, Trypsin
9.	**Vitamins**	Yeast, Shark liver oil, Shark liver oil, Amla, Oxytocin
10.	**Triterpenes**	Rasna, Colocynth
11	**Hormones**	Insulin

5.1.6 Chemotaxonomic Classification

The character most often studied in chemotaxonomy is secondary metabolites of pharmaceutical significance such as alkaloids, glycosides, and flavonoids. DNA hybridization, amino acid sequencing in proteins, and serotaxonomy are also gaining significance in this method of classification. This system of classification relies on the chemical similarity of a taxon, i.e., it is based on the existence of relationship between constituents in various plants. There are certain types of chemical constituents that characterize certain classes of plants (Solanaceae family contains tropane alkaloids, Apiaceae family contains volatile oil, Pinaceae family contains oleoresin, etc.). This gives birth to the entirely new concept of chemotaxonomy that utilizes chemical facts or characters for understanding the taxonomical status, relationships, and the evolution of the plants. For example, tropane alkaloids, volatile oils, and oleoresin generally occur among the members of Solanaceae, Apiaceae, Pinaceae families, respectively, and thereby serve as a chemotaxonomic marker of respective family. The berberine alkaloid in Berberis and Argemone; rutin in Rutaceae members, ranunculaceous alkaloids among Ranunculaceae members, etc., are other examples. Thus, the chemical examinations of different plants have established that there is close link between their chemical constituents and taxonomical status. Chemotaxonomic classification is the latest system of classification and it gives more scope for understanding the relationship between chemical constituents, their biosynthesis, and their possible action.

Chemical characters show chemical relationship, in the same way as morphological characters show morphological relationships. The chemical characters have taxonomic value as they are stable, unambiguous, and not easily changeable. Phytochemical data are more basic and more privileged and are more indicative of

relationship than morphological characters. But it is laborious and needs extensive analytical work.

Information from different sources should be taken into consideration to get a satisfactory classification of crude drugs, and there is no obvious advantage in attaining overriding importance to any one type.

5.2 Classification of Modern or Allopathic Drugs

The term 'allopathy' refers to the principle of curing a disease by administering substances that produce the opposite effect of the disease when given to a healthy human. The classification of allopathic drugs used in the Western world based on the clinical usage is considered to be straight forward. Allopathic drugs may be grouped in the following way:

(a) Non-prescription drugs—Non-prescription drugs are the drugs, which can be purchased from a pharmacy without the prescription of a doctor. These drugs are also called as over-the-counter drugs.
(b) Prescription drugs—Prescription drugs require a prescription from a registered physician before they can be purchased at the pharmacy. These drugs are not sold over the counter. This distinction clearly indicates the importance of medical advice for drug use and is governed by legislation. Over-the-counter drugs are safe to use in most cases excepting deliberate misuse or abuse.

The anatomical therapeutic chemical (ATC) classification system, recommended by the World Health Organization (WHO 2005), categorizes drugs into 14 main classes according to the organ or biological system they act on as well as their therapeutic, pharmacological, and chemical properties. For example, (i) alimentary tract and metabolism, (ii) blood and blood forming organs, (iii) cardiovascular system, (iv) dermatologicals, (v) genitourinary system and sex hormones, (vi) systemic hormonal preparations, excluding sex hormones and insulins, (vii) antiinfectives for systemic use, (viii) antineoplastic and immunomodulating agents, (ix) musculoskeletal system, (x) nervous system, (xi) antiparasitic products, insecticides and repellents, (xii) respiratory system, (xiii) sensory organs, and (ivx) various.

Different Groups of Allopathic Medicines

Based on the properties and uses, the allopathic drugs are also classified as antibiotics, antacids, antigas medicines, wormicides, steroid medicines, medicines for the external uses, antiallergens and antihistamines, antihypertensive, antidiabetic, antidiarrheal medicines, laxatives, medicines for anti cold and cough, antiepileptic, antispasmodic, antipyretics, analgesics, antivomiting, antiulcer, hematinic, tranquillizers, medicines for guddiness, enzymes, vitamins, mineral compounds, amino acids, etc.

Some of the examples of non-prescription and prescription drugs are listed below:

(i) **Antihemorrhoid drugs**: Antihemorrhoid drugs are medicines that reduce the swelling and relieve the discomfort of hemorrhoids. Antihemorrhoid drugs are available as creams, ointments, and suppositories. Most can be bought without a physician's prescription.

(ii) **Topical antibiotics**: Allopathic medicines like topical antibiotics are getting unique importance in healing wounds and inflammation. Topical antibiotics are medicines applied to the skin to kill bacteria. Topical antibiotics help in preventing infections caused by bacteria that get into minor cuts, scrapes, and burns. For example, neomycin, silver sulfadiazine with chlorhexidine gluconate, and povidone-iodine are powerful ointments for healing wounds. Treating minor wounds with antibiotics allows quicker healing. If the wounds are left untreated, the bacteria will multiply, causing pain, redness, swelling, itching, and oozing. Most can be bought without a physician's prescription.

Other allopathic drugs for topical application include betamethasone combined with neomycin, gentamycin, miconazole, and beclomethasone dipropionate combined with gentamycin sulfate which are some steroid creams to overcome skin inflammations and diseases. Skin irritations and inflammations throughout the body can be controlled by the application of lindane lotion. Calamine and diphenhydramine lotion is useful to overcome the skin irritations due to sunburns, prickly heat, and insect bites. Diclofenac diethylamine and diclofenac sodium are effective in body and joint pain relief. Methyl salicylate is also combined with above said two compounds to have effective treatment. Ichthammol glycerine is also applied to get relief from pain at a particular point of our body. Clotrimazole, beclomethasone dipropionate, gentamycin sulfate, iodochlorhydroxyquinoline, chlorocresol, benzyl alcohol, methylparaben, and propylparaben are some of the medicines used in the manufacturing of skin creams to get rid of skin infections. The mixture of clindamycin phosphate USP, sodium methylparaben I.P, and sodium propylparaben I.P (erytop) is effective in controlling pimples and acne. Face wash before the application of above said face cream will be useful to have a good result.

(iii) **Antibiotics**: Antibiotics are medicines which arrest the growth of bacteria or fungi in the human body. Usually, they are available in various forms such as dispersible tablets, capsules, syrups, drops, injections, and dry syrups. Penicillin (*Penicillium*) and streptomycin (*Streptomyces*) are two known antibiotics of fungal origin. A large varieties of antibiotics widely used as allopathic drugs are known including amoxycillin, ampicillin, cefadroxil, cephalexin, cloxacillin, tetracycline, gentamycin, erythromycin stearate, sulfamethoxazole, trimethoprim, norfloxacin,

ofloxacin, cefixime, cefpodoxime proxetil, gatifloxacin, rifampicin, isoniazid, metronidazole, etc.

Most of the antibiotics are combined with antiallergic medicines like cetirizine hydrochloride and chlorpheniramine maleate to get good result and to ensure our safety. Ampicillin and amoxycillin are combined with cloxacillin to get more effect when they are taken for curing bacterial infections. Sulfamethoxazole, trimethoprim, and norfloxacin are effective in controlling the urinary tract infections (many people will get allergic problem with sulfa drugs). Rifampicin and isoniazid are effective in controlling tuberculosis caused by mycobacteria. Amoxycillin and ampicillin are commonly available in the strength of 250 and 500 mg. It is advisable to take lower strength of antibiotics to ensure our basic immunity power.

(iv) **Cough suppressants**: Cough suppressants are medicines that prevent or stop coughing. Cough suppressants act on the center of the brain that controls the cough reflex. They are meant to be used only to relieve dry, hacking coughs associated with colds and flu. They should not be used to treat coughs that bring up mucus or the chronic coughs associated with smoking, asthma, emphysema, or other lung problems. Chlorpheniramine maleate, ammonium chloride, and sodium citrate are the effective formula to control cough. Sometimes, chlorpheniramine maleate is replaced by diphenhydramine hydrochloride to get another formula. Dextromethorphan hydrochloride, phenylpropanolamine hydrochloride, and triprolidine hydrochloride are other mostly used things for cough formula. To overcome dry irritating cough, guaifenesin is combined with salbutamol sulfate. The combination of codeine phosphate 10 mg I.P and chlorpheniramine maleate 4 mg I.P in syrup form is finding nice result in controlling dry cough. Terbutaline sulfate and bromhexine hydrochloride are also used to control cough problem in the allopathic medication. Most can be bought with a physician's prescription.

(v) **Antiacne drugs**: Antiacne drugs are medicines that help clear up pimples, black heads, white heads, and more severe forms of acne. Different types of antiacne drugs are used for different purposes. For example, lotions, soaps, gels, and creams containing benzoyl peroxide or tretinoin may be used to clear up mild to moderately severe acne. Isotretinoin is prescribed only for very severe, disfiguring acne.

(vi) **Non-steroidal and steroidal antiinflammatory drugs**: Non-steroidal antiinflammatory drugs are medicines that relieve pain, swelling, stiffness, and inflammation. Non-steroidal antiinflammatory drugs (NSAIDs) are prescribed for a variety of painful conditions, including arthritis, bursitis, tendinitis, gout, sprains, strains, and other injuries. Non-steroidal antiinflammatory drugs relieve pain, stiffness, swelling, and inflammation, but they do not cure the diseases or injuries

responsible for these problems. Physician's prescription is necessary for dispensing such drugs.

Salbutamol, betamethasone, theophylline, and dexamethasone are some of the steroid drugs with antiinflammatory effects. They can reduce inflammative conditions such as redness, swelling, and soreness. They are also helpful for many conditions such as asthma and arthritis. They come in pills, sprays, creams, and ointments. The creams and ointments of steroids are applied on skin to get rid of eczema and contact dermatitis. The side effects of steroid medicines are weakening bones, thinning of skin, and increasing blood sugar level. They also affect liver when excessively used. When salbutamol (asthalin inhaler) inhaled, it is very important to have self control in dosage, and beyond limit, it may affect heart.

(vii) **Antiseptics**: Antiseptics are medicines that slow or stop the growth of germs and help prevent infections in minor cuts, scrapes, and burns. Antiseptics are applied to the skin to keep bacteria from getting into wounds and causing infection. Although antiseptics do not usually kill bacteria, they do weaken them and slow their growth. Simply applying an antiseptic to a wound is not adequate treatment. The wound should be cleaned first, and in most cases, it should be covered with a bandage or other type of dressing to keep it clean and moist while it heals. However, some antiseptics, such as phenol, can damage the skin if the wound is covered after they are applied. Some of the drugs can be bought without a physician's prescription.

(viii) **Laxatives**: These are the drugs for the condition of constipation, mostly needed by the sick and old people. These should be used only in the unavoidable condition. One should not get addicted to these medicines. To correct motion in the natural way, we need only vitamins and amino acids. Bisacodyl 5 mg I.P in tablet form is useful for the treatment. Liquid paraffin and milk of magnesia are other liquid forms of laxatives.

(ix) **Antiepileptic medicines**: It is not a disease, but a sign of problem in the brain which is causing a disruption in the brain's normal electrical activity. It may occur in any age in either sex. The condition is called as 'fits.' Phenobarbitone (30 or 60 mg) I.P (gardinol), sodium valproate 200 mg I.P (valparin), carbamazepine 200 mg I.P, (tegretol), pentoxifylline B.P 400 (trental) mg, etc., are some of the antiepileptic medicines.

(x) **Analgesics**: Analgesics are medicines that relieve pain. Analgesics are prescribed to relieve pain of all sorts—headaches, backaches, joint pain, sore muscles, and pain that results from surgery, injury, or illness. Among the most common analgesics are aspirin, choline salicylate, magnesium salicylate, and sodium salicylate. Ibuprofen, naproxen sodium, and ketoprofen are non-steroidal antiinflammatory drugs (NSAIDs). NSAIDs relieve pain and also reduce inflammation. Another common analgesic, acetaminophen provides pain relief but does not reduce inflammation.

(xi) **Antispasmodic medicines**: Dicyclomine hydrochloride 100 mg I.P (cyclopam), hyoscine butylbromide 10 mg I.P (buscopan), and chlordiazepoxide 10 mg I.P (librax) are used for the stomach pain. Of which dicyclomine hydrochloride 100 mg I.P is combined with nimesulide 100 mg I.P and mild dose of B complex vitamin to control mensural pains for ladies.

(xii) **Decongestants**: Decongestants are medicines used to relieve nasal congestion (stuffy nose). A congested or stuffy nose is a common symptom of colds and allergies. This congestion results when membranes lining the nose become swollen. Decongestants relieve the swelling by narrowing the blood vessels that supply blood to the nose. This reduces the blood supply to the swollen membranes, causing the membranes to shrink.

(xiii) **Salicylates**: Salicylates are medicines that relieve pain and reduce fever. Aspirin belongs to this group of drugs. Other members of this group include sodium salicylate, choline salicylate, and magnesium salicylate. Aspirin is used to relieve many kinds of minor aches and pains—headaches, toothaches, muscle pain, menstrual cramps, the joint pain from arthritis, and aches associated with colds and flu. Aspirin is also known as acetylsalicylic acid.

(xiv) **Vasodilators**: Vasodilators are medicines that act directly on muscles in blood vessel walls to make blood vessels widen (dilate). Vasodilators are used to treat high blood pressure (hypertension). By widening the arteries, these drugs allow blood to flow through more easily, reducing blood pressure. Amlodipine, nifedipine, atenolol, and reserpine are some of the medicines used for hypertensive condition. These medicines block the transport of calcium into the smooth cells lining the coronary arteries and other arteries of the body. Since calcium is important in muscle contraction, blocking of calcium transport relaxes artery muscles. So these medicines are helpful to cure chest pain called as angina. Dizziness, muscle and stomach pain, and head ache are some of the side effects of these medicines.

(xv) **Antidiabetic drugs**: Diabetes is caused by the lack of secretion of insulin hormone from pancreas. The lack of insulin affects sugar metabolism and a considerable rise in blood sugar level. Some of the medicines taken for diabetes are as follows:
Sulfonylureas group of medicines (acetohexamide, chlorpropamide, glipizide, glyburide, etc.) help the body to make more or required insulin. Metformin helps control sugar by optimizing the body use of insulin and by reducing the amount of sugar that the body absorbs from food. Thiazolidinediones, pioglitazone, and rosiglitazone help the body use insulin better alike metformin and also helpful to produce less sugar when the food taken. Meglitinides help the body to make more insulin; nateglinide and repaglinide are usually taken with meals. Alpha-glucosidase inhibitors help the body absorb sugar more slowly

and keep the level of the sugar in normal. These are taken every time after the meals. Acarbose and miglitol are two kinds of medicines in this group. Glibenclamide is available in pills form in 5 mg strength, commonly prescribed for the initial stage of diabetes. Side effects are nausea and allergic reactions. This medicine should be avoided in case of severe dysfunction of liver and kidney, pregnancy, and breast feeding.

(xvi) **Antacids**: Antacids are medicines that neutralize excess acid in the stomach. Overeating and improper and missing diets are some reasons for the secretion of excess acid in the stomach. Antacids are used to relieve acid indigestion, sour stomach, gastric problems, peptic ulcers, and heartburn. Antacids contain ingredients such as aluminum hydroxide, calcium carbonate, magnesium hydroxide, and sodium bicarbonate, alone or in various combinations. Some antacid products also contain the ingredient simethicone to relieve gas. Antacids are taken by mouth and work by neutralizing excess stomach acid. They are available in both tablet and gel form.

(xvii) **Expectorants**: Expectorants are drugs that loosen and clear mucus and phlegm from the respiratory tract. Guaifenesin is an ingredient in many cough medicines, such as Anti-Tuss, Dristan Cold and Cough, Guaifed, Guai Cough, and some Robitussin products. Some products that contain guaifenesin are available only with a physician's prescription; others can be bought without a prescription. They come in several forms, including capsules, tablets, and liquids.

(xviii) **Antifungal drugs**: Fungi cause fungal infections. These fungi surround us and frequently land on our skin and are inhaled into our lungs. Many fungi are harmless, some cause minor and irritating infections, while a few can cause much more severe infections. People with compromised immune systems, such as AIDS and cancer patients, may be more susceptible to fungal infections than others. Antifungal drugs are used to treat fungal infections.

(xix) **Antiallergic and antihistamines**: Antiallergic drugs are used for relieving from allergic conditions. Allergy is a reaction of our immune system in response our body's contact with allergy making things called allergens. The allergens are not really harmful to all people. Naturally, our immune system, only in particular cases, wrongly decides that they are harmful. Antiallergic drugs include cetirizine hydrochloride, chlorpheniramine maleate, decongestant, antihistamines, antiinflammatory agents, and antileukotrienes. These antiallergy medicines can be consumed in the form of tablets, syrups, powder, and drops. When consumed, these antiallergic medicines support the immune system and improve its overall resistance against allergens. Antihistamines are drugs that block the action of histamine (a compound released in allergic inflammatory reactions) at the H1 receptor sites, responsible for immediate hypersensitivity reactions such as sneezing and itching. By inhibiting the activity of histamine, they can reduce capillary fragility,

which produces the erythema, or redness, associated with allergic reactions. They will also reduce histamine-induced secretions, including excessive tears and salivation. Antihistamines help stop allergy symptoms such as itchy eyes, sneezy, and runny nose. Sometimes, itchy rashes may also be helped by an antihistamine. Drowsiness, dry mouth, and blurry vision are some of the side effects of antihistamines. When taken, it is better to avoid driving, riding, and machinery operations.

(xx) **Antidiarrheal drugs**: Diarrhea is usually caused by the intake of contaminated food or drink with bacteria, virus, and parasites. Indigestion also will become the reason for the diarrhea. Loperamide 2 mg I.P is commonly used to overcome the condition. Quiniodochlor tablets (enteroquinol) are the other one to control diarrhea. Metronidazole 200 mg or in 400 mg is added with antidiarrheals to have quick arrest of diarrhea. To get relief from stomach pain, dicyclomine hydrochloride 100 mg I.P is added.

(xxi) **Antigas agents**: Antigas agents are medicines that relieve the uncomfortable symptoms of too much gas in the stomach and intestines. Phazyme and simethicone are some of the important medicines which are working against gas. They help relieve the symptoms by preventing the formation of gas pockets and breaking up gas that already is trapped in the stomach and intestines. Antigas agents are sold as capsules, liquids, and tablets (regular and chewable) and can be bought without a physician's prescription.

(xxii) **Smoking cessation drugs**: Smoking cessation drugs are medicines that help people stop smoking cigarettes or using other forms of tobacco. People who smoke cigarettes or use other forms of tobacco often have a difficult time when they try to stop. Most smoking cessation products contain nicotine, but the nicotine is delivered in small, steady doses spread out over many hours. Smoking cessation drugs that contain nicotine are also called nicotine substitution products or nicotine replacement therapy. These come in four forms—chewing gum, skin patch, nasal spray, and inhaler. Another type of smoking cessation drug, bupropion (zyban), also reduces craving and withdrawal symptoms, but it contains no nicotine.

(xxiii) **Enzymes**: These are the protein molecules which are naturally secreted from the pancreas to digest food. Pepsin I.P (1:3000) and α-amylase I.P (1:2000) are some of the important digestive enzymes. These are available in both capsule and liquid form. Lack of appetite, gastric problems, and indigestion needs enzymes.

(xxiv) **Wormicides**: Mebendazole and albendazole are important wormicides used in the allopathic medication. Mebendazole is used to overcome amebiasis, and albendazole is effective in vanishing worms found in human bowl and stomach. Albendazole is available in both chewable and liquid form. The people who are interested in nonvegetarian food

items need to use it to avoid worm problems. Loss of weight, lack of appetite, and anal itching are some of the symptoms of worm infections.

(xxv) **Vitamins**: Vitamins are very important for the essential activities of the body. Vitamin A, B complex (B1, B2, B6, B12), C, D, E, and K are some of the important vitamins used in the allopathic medication. Generally, vitamins are available in the form of capsules, tablets, syrups, and injections. They are used either separately or in mixed form. Vitamin A, retinol, is a growth-promoting and antiinfectant vitamin. It is naturally available in carrot, cabbage, grapes, fishes, and cod-liver oil. It is available in tablet and liquid form. Vitamin A increases appetite and sexual desire. Sight problem, skin problem, body weakness, and nervous complaint can be prevented by the addition of vitamin A. Vitamin B complexes are neurotrophic vitamins. They increase appetite. Vitamin B1 (thiamine mononitrate) and vitamin B2 (riboflavine) are used in the treatment of mouth ulcers. Vitamin B6 (pyridoxine hydrochloride) is taken for general health and good natural sleep. Vitamin B12 (cyanocobalamine) is obtained from animal part and used for having good body health and widely used in injection form. Vitamin C (ascorbic acid) is naturally found in citrus fruits, vegetables, and spices like pepper. It is useful to get rid of scurvy disease. It increases appetite and being an antioxidant keeps the health of skin and provides the young looking. Vitamin D (secosteroids—ergocalciferol, cholecalciferol, etc.) may be produced in the skin, specifically cholecalciferol from cholesterol in the presence of evening sunshine (hence its nickname, the 'sunshine vitamin'), and it is helpful to the growth of bones. Vitamin E (tocopheryl acetate) is, important for sexual and skin health, naturally available in badam nuts. Vitamin K (K1-phylloquinone, K2-menaquinone) is needed for the blood clotting in case of severe wounds and thus helps to avoid the loss of blood.

(xxvi) **Mineral compounds**: A variety of mineral salts are used in the medicine world. Ferrous gluconate, calcium carbonate, magnesium oxide, manganese sulfate, copper sulfate, zinc sulfate, sodium borate, and sodium molybdate are some of them. Calcium carbonate is used for the growth of the bones. Ferrous gluconate is used to overcome anemic problem, and it is combined with other minerals and vitamins when in use. Zinc sulfate is also very important for the health, and it induces sexual desire and increases immunity power. Sodium chloride, potassium chloride, and sodium nitrate are used to prepare salt mixture to overcome tiredness and dehydration because of diarrhea. Excess loss of minerals can be adjusted by the addition of this salt mixture dissolving in the ratio of 4.2 gm/200 ml of water. Sodium chloride and dextrose are used to prepare saline water for injection through veins.

(xxvii) **Amino acids**: Amino acids are essential for our nervous system. They increase our memory power, general health, and appetite. Alanine, arginine, asparagine, aspartic acid, cysterine, glutamic acid, glutamine,

glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine are required amino acids in daily food. There are about 20 varieties of amino acids in the medical science. Unlike fat and starch, these acids cannot be stored by our body for longer use. It is necessary to take enough amino acids in on regular basis.

(xxviii) **Antipyretics**: These are body temperature reducing medicines in case of high fever. Paracetamol, mefenamic acid, and nimesulide are some of the common antipyretics used in the allopathic world. These things work well when taken along with warm water. The over dose of paracetamol and nimesulide is susceptible to make liver and kidney problems, respectively. However, the adequate water drinking will be helpful to avoid such risks.

(xxix) **Analgesic medicines**: These are all body pain killer medicines. Paracetamol, ibuprofen, nimesulide, mefenamic acid, diclofenac sodium, diclofenac potassium, serapeptidase, aceclofenac, and chlorzoxazone are some of the important pain killers. These medicines are usually combined with neurotrophic vitamins, B complex, to have better result. Paracetamol suits well for headaches and nimesulide for tooth ache and body pain. Diclofenac sodium and serapeptidase are used for total body pain. Diclofenac potassium and chlorzoxazone are given for arthritis.

(xxx) **Antivomiting medicines**: Some people may be suffering from vomiting during their travelling time. Promethazine theoclate 25 mg I.P (avomine) is used to overcome vomiting problem during the travel; vomiting accompanied with fever can be cured by the intake of metoclopramide 10 mg I.P, nimesulide 100 mg I.P and ibuprofen + paracetamol tablets. Domperidone 10 mg is also taken instead of metoclopramide to cure vomiting.

(xxxi) **Antiulcer medicines**: Excess acid secreted because of overeating and missing of diets in correct time are the main reasons for ulcer problems. Indigestion associated with gas and heart burns is called as gastric ulcer. This condition is managed with antacid gel and ranitidine 150 mg I.P tablet. When the damages are found in the linings of stomach and small intestines because of the acidity, the condition will be called as peptic ulcer. Omeprazole 20 mg I.P or rabeprazole 20 mg I.P or pantoprazole 40 mg I.P or lansoprazole 30 mg I.P are accompanied with antacid and ranitidine tablets to get relief from peptic ulcer.

(xxxii) **Medicines for giddiness**: Prochlorperazine maleate 5 mg I.P, betahistine dihydrochloride 8 mg I.P (Vertin), and cinnarizine 25 mg I.P (Vertigon) are used to over come guddiness problems.

(xxxiii) **Tranquillizers**: Tranquillizers are the medicines which induce or bring the sleeping condition of the body. Diazepam 5 or 10 mg I.P, nitrosum 5 or 10 mg I.P, and alprazolam 0.25 or 0.5 or 1 mg I.P are some of the tranquillizers used in the allopathic medication. These medicines should be never taken with liquors as the presence of liquors in our body will

send 10–15 times greater than the normal sleeping pulses sent to brain by these medicines.

(xxxiv) **Hematinic medicines**: These are helpful to increase hemoglobin level of blood in our body. 'Hem' refers iron and 'globin' refers protein part of the blood. These medicines are containing iron compounds such as ferrous gluconate, ferric ammonium citrate, and iron choline citrate with protein hydrolysate, vitamin C, and vitamin B complex. The hematinic medicines are available in the form of capsules, tablets, and syrups.

5.3 Nutraceuticals, Functional Food, and Cosmeceuticals

Nutraceuticals and Their Classification

The term 'nutraceutical' was coined from 'nutrition' and 'pharmaceutical' in 1989 by Stephen L. De Felice (Jack 1995; Mannion 1998) and was originally defined as 'a food (or part of the food) that provides medical or health benefits, including the prevention and/or treatment of a disease' (Brower 1998; Kalra 2003, Trottier 2010). A nutraceutical may be a naturally nutrient-rich food (e.g., spirulina, garlic, soy) or a specific component of a food (e.g., omega-3 fatty acids, lycopene, saponins). They are also known as medical foods, 'designer foods,' nutritional supplements, and dietary supplements and include a number of substances ranging from natural diets, herbal products, biofortified crops, and genetically modified and processed food products such as cereals, soups, and beverages. Nutraceuticals can deliver benefits beyond basic nutrition and provide health benefit, modulate immunity, and/or prevent and cure specific diseases. The ability of nutraceuticals to influence chronic diseases (e.g., diabetes, cancers) has been recognized, and they will play important role in future therapeutic development. In addition, it is also claimed that nutraceuticals delay the aging process, increase life expectancy, or support the structure or function of the body. Herbal nutraceutical is useful in maintaining health, and it works against nutritionally induced acute and chronic diseases and promotes optimal health, longevity, and quality of life (Chauhan et al. 2013).

Nutraceuticals have received considerable interest because of their presumed safety and potential nutritional and therapeutic effects (Rajasekaran et al. 2008). People can improve their health by supplementation and by consuming foods that have been formulated or fortified. Another reason for the growing trend of nutraceuticals is public education, renewable source, cultivation and processing, environmental friendliness, and local availability (Keservani et al. 2010). UK, Germany, and France were the first who considered that diet is more important factor than exercise or hereditary factors in achieving a good health. Canada defined them as 'a product produced from foods but sold in pills, powders, (potions) and other medicinal forms not generally associated with food.' In India, nutraceuticals are the food components made from herbal or botanical raw materials, which are used for preventing or treating different types of acute and chronic maladies (Thakur et al. 2010).

Commercial nutraceuticals have to pass through strict regulatory controls for quality and positive health impact.

Classification of Nutraceuticals

Nutraceuticals are classified as traditional or natural nutraceuticals (e.g., nutrients, herbals, phytochemicals, probiotic picroorganisms, nutraceutical enzymes) and non-traditional or artificial nutraceuticals (e.g., fortified and recombinant nutraceuticals).

1. **Traditional nutraceuticals**

Traditional nutraceuticals are simply natural with no changes to the food. Food contains several natural components that deliver benefits beyond basic nutrition, such as lycopene in tomatoes, omega-3 fatty acids in salmon, or saponins in soy. Traditional nutraceuticals are grouped on the basis of (a) chemical constituents: (i) nutrients, (ii) herbals, and (iii) phytochemicals; (b) probiotic microorganisms; and (c) nutraceutical enzymes.

(a) Chemical constituents

(i) Nutrients

Substances such as vitamins, minerals, amino acids, and fatty acids with established nutritional functions. Most vegetables, wholegrain cereals, dairy products, fruits, and animal products such as meat and poultry contain vitamins and are helpful in curing heart diseases, stroke, cataracts, osteoporosis, diabetes, and cancer. Minerals found in plant, animal, and dairy products are useful in osteoporosis and anemia; build strong bones, teeth, and muscles; improve nerve impulses and heart rhythm. Flax seed and salmon contain fatty acids omega-3 PUFAs and are potent controllers of the inflammatory processes, maintenance of brain function, and reduce cholesterol deposition.

(ii) Herbals

Nutraceuticals hold a great promise to improve health and prevent chronic diseases with the help of herbals. Some examples are willow bark (*Salix nigra*), having active component as salicin, which is antiinflammatory, analgesic, antipyretic, astringent, and antiarthritic (Ehrlich 2009). Parsley (*Petroselinum cripsum*) contains flavonoids (apiol, psoralen) and is diuretic, carminative, and antipyretic. Peppermint (*Mentha piperita*) contains menthol as an active component and cures cold and flu (Ehrlich 2009). Lavender (*Lavandula angustifolia*) contains tannin which is helpful in curing depression, hypertension, stress, cold, cough, and asthma. Cranberries (*Vaccinium erythrocarpum*) contain proanthocyanidin and are found to be useful in cancer, ulcers, and urinary tract infections.

(iii) Phytochemicals

Phytochemicals constitute a class of nutraceuticals. They are classified on the basis of chemical name given according to their phytochemical properties. For example,

carotenoids (isoprenoids) found in various fruits, vegetables, and egg yolk are anticarcinogenic; boost natural killer immune cells; and protect cornea against UV light. Legumes (chickpeas and soybeans), grains, and palm oil contain non-carotenoids, which remove cholesterol and are anticarcinogenic. Flavonoid polyphenolics are found in berries, fruits, vegetables, and legumes, which are potent antioxidants and phytoestrogens; prevent breast cancer and prostate cancer; and control diabetes. Non-flavonoid polyphenolics are present in dark grapes, raisins, berries, peanuts, and turmeric roots; are strong antiinflammatory, antioxidants, and effective anticlotting agents; and reduce cholesterol. Phenolic acids, found in blueberries, tomatoes, and bell peppers having antioxidant activity, reduce mutagenicity of polycyclic aromatic hydrocarbons. Seeds of *Barbarea verna*, broccoli contain isothiocyanates (glucosinolates) and have antitumorigenesis activity.

(b) Probiotic microorganisms

The scientific interest in probiotics boosted from the work of Metchnikoff to transform the toxic flora of the large intestine into a host-friendly colony of Bacillus bulgaricus was found by Hord (2008). 'Probiotics' mean 'for life' and are defined as live microorganisms, which when consumed in adequate amounts confer a health effect on the host (Michail 2006). They are friendly bacteria that promote healthy digestion and absorption of some nutrients. They act to crowd out pathogens, such as yeasts, other bacteria, and viruses that may otherwise cause disease and develop a mutually advantageous symbiosis with the human gastrointestinal tract (Holzapfel et al. 2001). They have an antimicrobial effect through modifying the microflora, preventing adhesion of pathogens to the intestinal epithelium, competing for nutrients necessary for pathogen survival, producing an antitoxin effect, and reversing some of the consequences of infection on the intestinal epithelium, such as secretory changes and neutrophil migration. Probiotics can cure lactose intolerance by the production of the specific enzyme (ß-galactosidase) that can hydrolyze the offending lactose into its component sugars (Pineiro and Stanton 2007). Some sources of probiotic microorganisms are mentioned in Table 5.8 (Holzapfel et al. 2001).

(c) Nutraceutical enzymes

Enzymes are an essential part of life, without which our bodies would cease to function. Those people who are suffering from medical conditions such as hypoglycemia, blood sugar disorders, digestive problems, and obesity eliminate the symptoms by enzyme supplements to their diet. These enzymes are derived from microbial, plant, and animal sources as given in Table 5.9:

2. **Non-traditional nutraceuticals**

Non-traditional nutraceuticals are artificial foods prepared with the help of biotechnology. Food samples contain bioactive components which are engineered

Table 5.8 Sources of probiotic microorganisms

Milk	Yoghurt	Fermented products	Human breast milk	GI tract	Vegetables/grains/fruits
Lactobacillus acidophilus, *L. lactis*	*L. delbrueckii subsp bulgaricus*	*L. casei*, *L. cellobiosus*, *L. curvatus*, *L. fermentum*, *L. helviticus*, *L. farciminis*	*L. reuteri*, *L. salivarius*	*L. gasseri*, *L. johnsonii*	*L. brevis*, *L. plantarum*
	Bifidobacterium adolescentis	*B. thermophilum*, *B. animalis*	*B. infantis*, *B. longum*, *B. breve*, *B. lactis*		
Propioni-bacterium freudenreichii	*Streptococcus thermophilus*	*Enterococcus faecium*, *Pediococcus acidilactici*		*Escherichia coli Nissle 1917*	*Leuconostoc mesenteroides*
					S. cerevisiae, *S. boulardii* Mushrooms

Table 5.9 List of nutraceutical enzymes from microbes, plants, and animals

Microbial enzymes/source	Plant enzymes/source	Animal enzymes/source
Hemicellulase (microorganisms and mushrooms)	Hemicellulase (plant walls)	Ox bile (ox)
Catalase	Pectinase (cell wall)	Pancrelipase (pancreatic juice)
Amyloglucosidase (ascomycetes)	α-Galactosidase (beans, cabbage, Brussels sprouts, broccoli, asparagus, other vegetables, and whole grains)	Trypsin (pancreatic juice)
Glucoamylase (*A. niger*, *Saccharomycopsis fibuligera*)	β-Amylase (higher plants)	Chymotrypsin (all classes of vertebrates)
Cellulase (all living cells)	Bromelain (pineapple)	Pepsin (animals tracheal secretions)
Invertase–Sucrase (yeast)	Biodiastase (soybean)	Lysozyme (saliva, tears, egg white, and many animal fluids)
Lactase–β-Galactosidase (bacteria)	Glucoamylase (callus and suspension cultures of sugar beets (*Beta vulgaris* L.) as well as in mature roots)	α–Amylase (saliva)

Source www.specialtyenzymes.com/

to produce products for human wellness. They are arranged into (i) Fortified nutraceuticals, (ii) Recombinant nutraceuticals, and (iii) Fortified nutraceuticals.

(i) Fortified nutraceuticals

It constitutes fortified food from agricultural breeding or added nutrients and/or ingredients, e.g., orange juice fortified with calcium, cereals with added vitamins or minerals, and flour with added folic acid. Some examples are milk fortified with cholecalciferol used in vitamin D deficiency (Casey et al. 2010). Prebiotic and probiotic fortified milk with *Bifidobacterium lactis* HN019 used in diarrhea, respiratory infections, and severe illnesses, in children (Sazawal et al. 2010). Banana fortified using soybean ferritin gene in iron deficiency was discovered by Kumar et al. (2011).

(ii) Recombinant nutraceuticals

Energy-providing foods such as bread, alcohol, fermented starch, yogurt, cheese, vinegar, and others are produced with the help of biotechnology. The production of probiotics and the extraction of bioactive components by enzyme/fermentation technologies as well as genetic engineering technology are achieved through biotechnology. Some of the products of recombinant organisms are shown in Table 5.10.

Table 5.10 Product produced by recombinant organisms (microorganisms, plants, and animals)

Product produced by recombinant microorganisms, plants, and animals			
A. Recombinant microorganisms			
Source	Enzyme	Products	References
Acetobacter xylinum	β-glucuronidase	Kombucha beverage	Malbasa et al. (2011)
Escherichia coli K-12	Chymosin	Milk-coagulated products	El-Sohaimy et al. (2010)
Fusarium venenatum	Xylanase	Increased bran solubilization	Sibbesen and Sorensen (2010)
Aspergillus oryzae	Esterase–lipase, aspartic proteinase, glucose oxidase, laccase, lipase, pectin esterase,	Alcoholic beverages (Sake, koji)	Ghorai et al. (2009)
Saccharomyces cerevisiae	Stilbene synthase and 4-coumaroyl-CoA	Resveratrol	White (2009)
Spirulina pacifica	Indoleamine 2,3-dioxygenase (IDO)	Increased hemoglobin	[www.nutraceuticalsworld.com/]

B. Recombinant plant			
Recombinant	Deficiency	Gene for recombination	References
Gold kiwifruit	Iron	High level of ascorbic acid, carotenoids lutein, and zeaxanthin	Beck et al. (2011)
Potatoes	Protein	Tuber-specific expression of a seed protein, *AmA1* (*Amaranth Albumin 1*)	Chakraborty et al. (2010)
Golden mustard	Vitamin A	Soybean *ferritin* gene	Chow et al. (2010)
Multivitamin corn	Multivitamin	Vitamins β-carotene corn (*Zea mays*) phytoene synthase (*psy1*) cDNA, ascorbate (rice dehydroascorbate reductase *(dhar*) cDNA, and folate *E. coli folE* gene encoding GTP cyclohydrolase (*GCH1*)	Naqvi et al. (2009)
Maize	Vitamin A (retinol)	Bacterial genes *crtB* and *crtI*	Aluru et al. (2008)
Tomato	Folate	Aminodeoxychorismate synthase (*AtADCS*)	de la Garza et al. (2007)
Golden rice	Vitamin A (retinol)	Two daffodil genes and one bacterial gene	Rockefeller Foundation www.rockfound.org
Iron rice	Iron deficiency	Soybean *ferritin* gene	[www.biotech.nature.com]

C. Recombinant animals			
Cattle	Human lysozyme	*rhLZ* expression vector *pBC2-HLY-NEOR*	Yang et al. (2011)
Yogurt	Probiotics microorganism	*Bifidobacterium lactis Bb-12* and *Lactobacillus acidophilus LA-5*	Allgeyer et al. (2010)
Cows	Lactoferrin deficiency	Recombinant human lactoferrin (rhLf)	Hyvonen et al. (2006)

Commercial Nutraceuticals

Many pharmaceutical companies are now trying to manufacture nutraceutical because there is undoubtedly a very huge and growing market. Nutraceuticals cover most of the therapeutic areas, such as antiarthritic, cold and cough, sleeping disorders, digestion and prevention of certain cancers, osteoporosis, blood pressure, cholesterol control, pain killers, depression, and diabetes. Recognition of health benefits from consumption of omega-3 rich seafoods is one of the most promising developments in human nutrition and disease prevention research in the past three decades (Pandey et al. 2010). Examples of some of the commercial nutraceutical manufacturers and their products name with expected claim are given below.

Bio Serae Laboratories of France manufactures 'Serenzo certified Organic' which constitutes citrus extract and acts as an antistress product; 'Resveravine' constitutes resveratrol and help in cardiovascular protection and antiaging properties [www.bioserae.com/]. Shotz Health of UK prepares 'Big Shotz' from ginseng, prebiotics rich in MEG-3 brand omega-3 EPA/DHA [http://www.nutraceuticalsworld.com/]. Guangzhou Lohas Biological Technology Co. Ltd. of China produces 'Ginseng KianpiPil' using reishi extract, ginseng extracts, and Rhodiola rosea extract as dietary supplement [www.company.indiatradepage.com/]. An Indian company, for example, La Casa Agrotech Private Ltd. manufactures 'Smrutihills' from Brahmi, Mandukaparni, as nervine tonic for mind and memory. SAB Herbals and Nutraceuticals assembles 'Methoxsalen Xanthotoxin Calcium Sennoside' from phytochemicals used in treating psoriasis, eczema, and vitiligo [www.hotfrog.in/Companies/].

Isha Agro Developers Pvt. Ltd. produces 'Imunohills' from amla, guduchi, and gokshura, which promotes cellular and humoral immunity. Bio Bodyfuelz Ltd. prepares 'PWR Sports' from *Sida cordifolia* extract which helps to boost endurance and refreshes muscles and 'Fat Burner' from cocoa beans extract (6% theobromine). Life Style Care produces 'Arctic Sea Super Omega' from olive oil and fish oil and is a rich source of omega-3 fatty acids and 'Forever Absorbent C' from bioflavonoids of oranges and papayas. Essential'z Energize Your Health manufactures 'Muscle Juice from protein blend' (whey protein isolate, whey protein concentrate, calcium caseinate, and egg white albumin) which feeds and nourishes the muscles. Amrutam Life Care Private Ltd. prepares 'Obexi' from *Boerhaavia diffusa* and is an antiobesity drug [www.trade.indiamart.com/].

Regulations

Food regulation is aimed at protecting the consumer's health, increasing economic viability, harmonizing well-being, and engendering fair trade on foods within and between nations. Commercial nutraceuticals have to pass through strict regulatory controls to provide a positive impact on an individual's health.

Functional Foods

There is no universally accepted definition of functional foods. Conventional foods generally satisfy nutritional function and hedonistic or sensory function of an individual, while functional foods fulfill specific physiological function beyond adequate nutritional effects in a way that is relevant to either an improved state of health and/or reduction in risk of disease. Functional foods can be considered to be those whole, fortified, enriched, or enhanced foods that provide health benefits beyond the provision of essential nutrients (Hasler 2002). Functional foods must remain foods and contain an ingredient (or fortified with an ingredient) like micronutrient or chemical with a beneficial effect on one or more target functions in the body beyond adequate nutritional effects (well-being or disease prevention); they must demonstrate their effects (or at least claim), and these effects can be expected to materialize when the food is consumed in normal amounts as part of the usual diet (but not be pills or capsules). A functional food can be a natural food, a fortified food, or a food from which a component has been removed by technological or biotechnological means, a food where the nature or bioavailability of one or more components has been modified, or any combination of these possibilities. A functional food might be functional for all members of a population or for particular groups of the population on the basis of age or genetic constitution.

There exists a direct relationship of diet to disease, and according to Willett (2002), over 60% of the risk of chronic diseases (e.g., heart disease, stroke, colon cancer, and type II diabetes) is potentially preventable by lifestyle modifications, including changes in diet. Based on the decades of scientific inquiry, the World Health Organization (WHO 2003) states that diet plays an important role in affecting the risk of a variety of chronic diseases and disorders (e.g., cancer, heart disease, type II diabetes, and obesity). There is continued interest in characterizing the contribution of diet to bone, joint, and eye health as well as to cognitive function. Increased consumption of fruits/vegetables is associated with a lowering of risk of a variety of cancers (Steinmetz and Potter 1996). For these and several other reasons (high healthcare costs, aging, health-conscious population, desire for healthy eating and lifestyle habits, changes in food regulations, numerous technological advances, growing marketplace for health-promoting products, etc.), interest in functional foods is growing worldwide. It is, however, not a new concept as the Ministry of Health, Labour and Welfare of Japan has been regulating Foods for Specified Health Uses (FOSHU) since 1080s with documented health benefits (Arai 1996; Nakajima 2004).

The foods might provide a therapeutic benefit is also not a new concept. The tenet, 'Let food be thy medicine and medicine be thy food,' was embraced ~2500 years ago by Hippocrates, the father of medicine. According to Roberfroid (2002), functional foods are generally part of a diet that provides health benefits beyond traditional nutritional effects. Functional foods have a potentially positive effect on health beyond basic nutrition. Functional foods promote optimal health and help reduce the risk of disease. For example, oatmeal is functional food because it contains soluble fiber that can help lower cholesterol levels and thereby reduce the risk of heart attack. Some foods are modified to have health benefits, e.g.,

orange juice that has been fortified with calcium for bone health. Health benefit is most likely due to the collective presence of many nutrient and non-nutrient plant components (a cocktail of phytochemicals). Glucosamine, calcium, and antiinflammatory and antioxidant nutrients, and phytochemicals are suggested for the improvement of joints, muscles, and bones. Role of xanthophylls (lutein) in eye health, conjugated linoleic acid (CLA) and tea phenolics in weight maintenance, and the balance between muscle mass and fatty tissue are suggested.

Consumption of refined and processed foods may trigger an immune response leading to inflammation which may contribute too many diseases and disorders from atherosclerosis to Alzheimer's disease. Some functional foods (e.g., fatty fish, whole grains, dark leaf greens, nuts, peppers, tomatoes, beets, ginger and turmeric, onions and garlic, and berries) with the help of their important minerals, fiber, vitamins, and other contents can reduce the risk of inflammation and many other diseases. Fatty or oily fish (e.g., salmon, tuna, sardines, and mackerel) is high in omega-3 fatty acids; whole grains (brown rice, steel cut oats, buckwheat and bulgur wheat) have more fiber than refined grains (white bread, white rice, and degermed cornmeal); dark leafy greens (e.g., broccoli, spinach, kale, collard greens, and rainbow chard) are a low-glycemic food, full of vitamin E, and have very high concentrations of minerals (Mg) and phytochemicals; almonds are full of fiber, vitamin E, calcium, omega-3s, and heart-healthy fat; bell peppers have capsaicin in them and are also full of important antioxidants; tomatoes are high in antioxidant and lycopene; beet root juice is high in antioxidants, fiber, vitamin C, and betalains; the antiinflammatory compound gingerol of ginger provides free radical protection, and curcumin of turmeric is a powerful antioxidant; berries (strawberries, blueberries, cranberries, etc.) are high in anthocyanins, the powerful antioxidants. They reduce the risk of inflammation, blood pressure, insulin spike, and many other diseases. Food products enriched for soy protein, plant sterols and stanols, omega-3 fatty acids, antioxidants, and fiber are being formulated and offered to the consumer (Meister 2002). The delivery of health benefits through functional food is a relatively new concept, and it is gaining in popularity in the society including producers (food industries) and consumers. However, the legal status with respect to food law is not yet well documented. Functional foods represent one of the most intensively investigated and widely promoted areas in the food and nutrition sciences today, but these are not magic bullets or panaceas for poor health habits (but diet), and linking the consumption of functional foods with health claims should be based on sound scientific evidence (Hasler 2002).

Scientists have identified the great majority of different physiologically active components in foods from plants (phytochemicals) and a few from animals (zoochemicals) or microbes that potentially could reduce the risk of a variety of chronic diseases. Characteristics of some functional foods available on the US market are shown in the following Table 5.11.

Like functional food, there are more terms for dietary products such as food supplements (or dietary supplements) and nutraceuticals (or nutriceuticals) that directly link nutrition with health.

Table 5.11 Strength of evidence for functional foods currently on the US market

Functional food	Bioactive component	Health benefit	Type of evidence	Strength of evidence	Recommended amount or frequency of intake	Regulatory status
1. Plant origin (phytochemicals)						
Fortified margarines	Plant sterol and stanol esters	Reduce total and LDL cholesterol	Clinical trials	Very strong	1.3 g/d for sterols 1.7 g/d for stanols	Health claim
Psyllium	Soluble fiber	Reduce total and LDL cholesterol	Clinical trials	Very strong	1 g/d	Health claim
Soy	Protein	Reduce total and LDL cholesterol	Clinical trials	Very strong	25 g/d	Health claim
Whole oat products	Glucan	Reduce total and LDL cholesterol	Clinical trials	Very strong	3 g/d	Health claim
Cranberry juice	Proanthocyanidins	Reduce urinary tract infections	Small number of clinical trials	Moderate	300 mL/d	Conventional food
Garlic	Organosulfur compounds	Reduce total and LDL cholesterol	Clinical trials	Moderate	600–900 mg/d	Conventional food or dietary supplement
Spinach, kale, collard greens	Lutein/zeaxanthin	Reduce risk of age-related macular degeneration	Epidemiological	Weak to moderate	6 mg/d	Conventional food or dietary supplement
Tomatoes and processed tomato products	Lycopene	Reduce risk prostate cancer	Epidemiological	Weak to moderate	Daily	Conventional food
Cruciferous, vegetables	Glucosinolates, indoles	Reduce risk of certain types of cancer	Epidemiological	Weak	3 or more servings/wk	Conventional food
Green tea	Catechins	Reduce risk of certain types of cancer	Epidemiological	Weak to moderate	Unknown	Conventional food

(continued)

Table 5.11 (continued)

Functional food	Bioactive component	Health benefit	Type of evidence	Strength of evidence	Recommended amount or frequency of intake	Regulatory status
2. Animal origin (zoochemicals)						
Fatty fish	(n-3) Fatty acids	Reduce TG, reduce heart disease cardiac deaths and fatal and non-fatal myocardial infarction	Clinical trials; epidemiological studies	Strong	2/wk	Qualified health claim for dietary supplements
Lamb, turkey, beef, dairy	CLA (conjugated linoleic acid)	Reduce breast cancer	In vivo and in vitro studies	Weak	Unknown	Conventional food
Fermented dairy products	Probiotics	Support GI (gastrointestinal) health, boost immunity	In vivo and in vitro studies, limited clinical data	Weak	Daily	Conventional food or dietary supplement

Source Hasler (2002)

Foods that have an FDA-approved health claim (sterol/stanol esters, oats, psyllium, soy) generally are supported by two dozen or more well-designed published clinical trials

Food supplements are concentrated sources of nutrients, dietary ingredients (including vitamins, minerals, amino acids, enzymes, glandulars, metabolites, organ, tissues, herbs, or other botanicals), or other substances with a nutritional or physiological effect whose purpose is to supplement the normal diet, available in the market in dose form (e.g., as pills, tablets, capsules, softgels, gelcaps, powders, extracts, or liquids in measured doses) taken by mouth and must not represent the product as a conventional food or a sole item of a meal or diet (EC 2007; FDA 2007).

Functional foods are similar in appearance to conventional foods and are consumed as part of a normal diet (Zeisel 1999), whereas the food supplements are not considered to be proper food. For nutraceuticals, the concept is less clear. A nutraceutical is a food or naturally occurring food supplement or part of a food that allegedly provides medicinal or health benefits, including the prevention and treatment of disease. A nutraceutical may be a naturally nutrient-rich or medicinally active food, such as garlic or soybeans, or it may be a specific component of a food, such as the omega-3 fish oil that can be derived from salmon and other cold-water fish.

A nutraceutical may be a product isolated or purified from foods, provides physiological benefit or protection against chronic disease, and is generally sold in medicinal forms not usually associated with foods (Canada 2007). Zeisel (1999) defines nutraceuticals as those diet supplements that deliver a concentrated form of a presumed bioactive agent from a food, presented in a nonfood matrix, and used to enhance health in dosages that exceed those that could be obtained from normal foods. The definition of nutraceuticals may be limited to natural, bioactive chemical compounds that have health-promoting, disease-preventing, or medicinal properties, or the concept may be extended by adding the category of medicinal foods (e.g., transgenic plants for oral vaccination against infectious diseases) to the other two nutraceutical categories of dietary supplements (e.g., vitamins, minerals, and plant extracts) and functional foods (e.g., omega-3 milk, cholesterol reducing oils and fats). According to these definitions, there is a clear distinction between functional food and food supplements, while nutraceuticals can cover functional food and food supplements, i.e., both functional food and food supplements could be considered nutraceuticals—as long as they can be derived from natural sources.

Classification of Functional Foods

Functional food may be classified into several groups on the basis of (i) food group it belongs to (e.g., dairy products, beverages, cereal products, confectionary, oils, and fats); (ii) the diseases it is expected to prevent or alleviate (e.g., diabetes, osteoporosis, colon cancer); (iii) its physiological effects (e.g., immunology, digestibility, antitumor activity); (iv) the category of its specific biologically active ingredients (e.g., minerals, antioxidants, lipids, probiotics); (v) its physicochemical and organoleptic properties (e.g., color, solubility, texture); or (vi) the processes that are used in its production (e.g., chromatography, encapsulation, freezing) (Juvan et al. 2005).

The Future of Functional Foods

According to the Department of Health and Human Services, diet plays a role in 5 of 10 of the leading causes of death, including coronary heart disease (CHD), certain types of cancer, stroke, diabetes (noninsulin dependent or type 2), and atherosclerosis. The dietary pattern characterized by high total and saturated fat, cholesterol, sodium, and refined sugars and low unsaturated fat, grains, legumes, fruits, and vegetables has been linked with these major causes of death in many developed countries including the USA. It has been suggested that consumption of certain foods or their associated physiologically active components may be linked to disease risk reduction (Hasler 1998).

Extensive research activities by academic, government, and private research institutes across the world are currently going on to understand and explore the mechanism of action of functional foods against chronic diseases of consumers. Nutrigenomics, following the results of human genome sequence, will have a profound effect on future functional foods research and development and also on future disease prevention efforts including the future of the functional foods industry (Fogg-Johnson and Meroli 2000; Anonymous 2001). Biotechnology will also influence the future of functional foods (Gura 1999). For example, development of genetically engineered iron-enriched rice and golden rice help prevent iron deficiency anemia and vitamin A deficiency-related blindness of millions of worldwide (Anonymous 2000). In the future, other foods enhanced with other nutritive or nonnutritive substances may even help to prevent chronic diseases such as heart disease, osteoporosis, or cancer (Falk et al. 2002; Pande et al. 2010).

Cosmeceuticals

The term 'Cosmeceutical' is a hybrid combination of cosmetics and pharmaceuticals. Cosmeceuticals have medicinal benefits (but not just used for beautification), which affect the biological functioning of the organ concerned depending upon the type of functional ingredients they contain. Cosmeceuticals are cosmetic products containing biologically active ingredients to add medical or drug-like benefits (e.g., cream, lotion, and ointment containing botanical, animal, and marine extracts like antioxidants, vitamins, peptides, essential oils, waxes, oils, natural color, natural fragrances, parts of plants like leaves). Cosmetics containing botanicals are herbal cosmetics, and for herbal cosmetics, permissible cosmetic ingredients are taken to form the base, and one or more herbal ingredients are added to it. Trees and herbs like *Azadirachta indica*, *Cocos nucifera*, *Aloevera* spp., *Camellia sinensis*, *Calendula* spp., *Carica papaya*, *Curcuma longa*, *Cymbopogon* spp., *Daucus carota*, *Emblica officinalis*, *Eucalyptus* spp., *Ginkgo biloba*, *Helianthus annuus*, *Lawsonia inermis*, *Rhodiola rosea*, *Rosea* spp., and similar many other herbs possess a vast and complex arsenal of bioactive phytochemicals (e.g., vitamins, antioxidants, oils and essential oils, hydrocolloids, proteins, terpenoids) that are able to calm or smooth, clean, restore, heal, and protect the skin and other parts of the body.

Examples of some of the zoochemicals used in cosmetics include the following: (i) hyaluronic acid, produced from rooster combs (fleshy growth or crest on the top of the head of gallinaceous birds), is used in antiaging skin care products as it is an antioxidant and a humectant and boosts collagen synthesis; (ii) carmine, a red dye made of red pigment from the crushed female cochineal insect, is often used in lipsticks, rouge, eye shadow, etc., and also used in food and drinks; (iii) most collagen in skin care creams comes from chicken feet and animal horns, and loss of collagen is one of the main signs of facial aging; (iv) glucosamine is derived from chicken bone marrow for the cosmetics industry; (v) ambergris from sperm whale is used in cosmetics as a fixative; (vi) fake vanilla fragrance comes from cow dung; (vii) placental protein comes from animal placenta; (viii) animal-derived stearic acid derived comes from waste animal tissue of cow, pig, and sheep; (ix) crystalline guanine, extracted from fish scales, is used to produce shiny effect in shampoo, eye shadow, and nail polish; panthenol, comes from meat or honey, is used in shampoos and conditioners to moisturize and lubricate hair; (x) keratin, hair care product, is extracted from horns, hooves, feathers, quills, and hair of various animals; and (xi) shellac, a resin secreted by the female lac insect, is used to create a shiny lacquer in products such as hairsprays, shampoos, mascara, and lipstick. Many of these chemicals are used as active ingredients of different cosmetic formulations for skin problems (like hyper pigmentation, skin wrinkling, skin aging, rough skin texture), hairspray, shampoo, etc.

Marine organisms including marine algae are rich sources of structurally diverse bioactive compounds like polyunsaturated fatty acids, pigments, and antioxidants for different biomedical products. A diverse group bioactive substances like terpenoids, carotenoids, tocopherol, phenolic compounds, polysaccharides (fucoidan, carrageenans, alginates, and agar), unsaturated fatty acids, mycosporine-like amino acids, and unsaturated fatty acids derived from marine algae are potential ingredients for cosmeceuticals (Agatonovic-Kustrin and Morton 2013). Many of these marine algae-derived compounds (vitamins, phytochemicals, enzymes, antioxidants, essential oils, etc.) are incorporated in skin care cosmeceuticals like creams, lotions, and ointments (Kim et al. 2008). These bioactive ingredients used in topical cosmeceuticals protect function like antioxidant, provide UV radiation protection, inhibit melanogenesis, immunomodulator, control of cutaneous bacterial flora, antiaging, antiwrinkle, antiviral, antiinflammatory, anticoagulant, antitumor, antihyperlipidemic agents, skin repair, skin hydration, gelling, and stabilizer. Functions of individual bioactive molecule or their group are given in Table 5.12:

Bioactive substances derived from marine resources have diverse functional roles as natural skin care agents, and these properties can be applied to the development of novel cosmetics as well as nutricosmetics from edible seaweeds and edible marine animals (Kim 2014).

The cosmeceuticals that are ingested orally are known as nutricosmetics. All these products are intended for the improvement of health and beauty of the skin and hair. They contain a wide spectrum of biologically active ingredients of natural origin including moisturizer, vitamin, sun protector, skin whitener, and free radical scavenger are nutritional supplements and support the function and the structure of

Table 5.12 Cosmeceutical application of compounds derived from marine algae

Bioactive component	Potential function as cosmeceutical	Other uses
1. Terpenoids	Photodamage, photoaging	
2. Carotenoids	UV filter, epidermal cells renewal, antioxidant, control of cutaneous bacterial flora	
3. Tocopherol	UV protection	
4. Phenolic compounds	UV protection	
5. Fucoidans	Antiaging, antiwrinkle	Antiviral, antiinflammatory, anticoagulant, antitumor
6. Carrageenans	Gelling and thickening	Antitumor, anticoagulant, immunomodulatory, antihyperlipidemic, induction of experimental inflammation and inflammatory pain, antiviral
7. Alginates	Face masks and body washes, skin repair, skin hydration, gelling, stabilizer	
8. Agars	Gelling, emulsifying	Bulking agent, laxative, anticoagulant, antioxidant
9. Unsaturated fatty acids	Antiaging, UV filters, antiwrinkle, regeneration, skin hydration	Antiinflammatory
10. Mycosporine-like amino acids	UV filters	

Source Agatonovic-Kustrin and Morton (2013)

the skin (e.g., vitamin C, omega-3 fatty acids, carotenes, flavonoids). Vitamin C functions as an antioxidant, reduces the impact of free radicals in the skin, and functions in the production of collagen in the dermis; omega-3 fatty acids and carotenes protect the skin from the damaging effects of ultraviolet light exposure, which may lead to accelerated skin aging and wrinkle formation (Katiyar 2002; Nichols and Katiyar 2010; Schagen 2012). Since 1990s, sales of nutricosmetics have increased dramatically to over 1 billion USD annually (Anonymous 2006). The various other terms by which cosmeceuticals can be substituted are active cosmetics, performance cosmetics, functional cosmetics, and dermaceuticals. Today's cosmeceuticals as well as nutricosmetics are serving as a bridge between personal care products and pharmaceuticals. The Cosmeceuticals are broad-spectrum topical agents that lie somewhere between pure cosmetics (lipstick and rouge) and pure drug (antibiotics and corticosteroids).

Classification of Cosmeceuticals

Cosmeceuticals are classified on the basis of their use into three categories as (a) skin cosmeceutical product (e.g., antiaging creams, moisturizers, facial products, and lotions); (b) hair cosmeceutical product (e.g., gel and creams, hair colorants and dyes, shampoos, growth stimulators, and conditioners); and (c) others (e.g., lipstick, nail polish, toothpaste, and powders). On the basis of the active ingredient content and function, cosmeceuticals are classified into eight categories as (a) retinoids (e.g., vitamin A, niacinamide, panthenol); (b) sunscreens (e.g., ferulic acid, enzophenones, dihydroxybenzone, oxybenzone, sulisobenzone); (c) moisturizers (e.g., emollients, Jojoba esters); (d) hydroxyacids (e.g., citric acid, malic acid, lactic acid); (e) depigmenting agents (e.g., hydroquinone, ascorbic acid, kojic acid, glabridin); (f) exfoliants (e.g., salicylic acid, lactic acid, glycolic acid); (g) antioxidants (e.g., α-lipoic acid, vitamins A, C, E, niacinamide, *N*-acetyl-glucosamine, α-tocopherol, lactobenzoic acid, ubiquinone, polyphenols); (h) proteins/peptides (e.g., pentapeptides-KTTKS); and (i) growth factors.

Classes of Cosmeceuticals

a. Skin cosmeceutical product—Antiaging creams, moisturizers, facial products, and lotions;
b. Hair cosmeceutical product—Gel and creams, hair colorants and dyes, shampoos, growth stimulators, and conditioners; and
c. Others—Lipstick, nail polish, toothpaste, and powders.

a. Skin cosmeceuticals

These cosmeceuticals are the cosmetic products that have medicinal or drug-like benefits are able to affect the biological functioning of skin owing to the type of functional ingredients they contain. These are skin care products that go beyond coloring and adorning the skin. Such products improve the functioning/texture of the skin by encouraging collagen growth by combating harmful effects of free radicals, thus maintaining keratin structure in good condition and making the skin healthier. OLAY vitamin line, which includes vitamins A, C, D, E, selenium, and lycopene, pycnogenol plus zinc and copper, is a well-known skin care line. The treatment of aging skin with a cream containing a hormone such as estrogen results in a fresh appearance with a rejuvenating effect. Kuno and Matsumoto (2004) had patented an external agent for the skin comprising an extract prepared from olive plants as a skin beautifying component, in particular, as an antiaging component for the skin, and/or a whitening component. Dry emollient preparation containing monounsaturated Jojoba esters was used for cosmeceutical purpose. Martin (2004) utilized plant extract of genus chrysanthemum in a cosmetic composition for stimulating skin and/or hair pigmentation (Preetha and Karthika 2009).

Commonly Used Skin Cosmeceuticals

(i) Hydroxy acid: Hydroxy acid also referred to as fruit acids; they are a common ingredient found in many cosmeceutical products. Examples include citric acid, malic acid, and lactic acid. AHAs improve skin texture and reduce the signs of aging by promoting cell seeding in the outer layers of the epidermis and by restoring hydration. AHAs also reduce the calcium ion concentration in the epidermis and the resulting reduction of the calcium ion levels tends to promote cell growth and slow cell differentiation, thus giving rise to younger looking.

(ii) Botanicals: Botanicals comprise the largest category of cosmeceutical additives found in the market place today. Some botanicals that may benefit the skin include green tea extract, ferulic acid, and grape seed extract.
Ferulic acid: This compound, which is derived from plants, is considered to be a potent antioxidant and has been shown to provide photo protection to skin. Furthermore, when ferulic acid is combined with vitamins C and E, the product has been shown to provide substantial UV protection for human skin. Moreover, Murray et al. (2008) reported that because its mechanism of action is different from sunscreens, ferulic acid could be expected to supplement the sun protection provided by sunscreens.
Grape seed extract: This botanical has been established as a potent antioxidant and has been shown to speed wound contraction and closure. Topical application of grape seed extract has also been shown to enhance the sun protection factor in humans.

(iii) Depigmenting agent: Skin-lightening agents added to product formulations have become increasingly popular, and such products are in demand. Common depigmenting ingredients include hydroquinone, ascorbic acid (vitamin C), kojic acid, and licorice extract (glabridin).
Hydroquinone: Hydroquinone has been the popular agent of choice for skin lightening. The US FDA has proposed concentrations between 1.5 and 2% in skin lighteners. A recent study suggests that this concern has been based mainly on studies with animal models utilizing long-term exposure at high dosages which are carcinogenic. Routine topical application may pose no greater risk than that from levels present in common foods.

(iv) Exfoliants: Exfoliants promote skin turnover by removing adherent cells in the stratum corneum. Common exfoliants found in cosmeceutical preparations include salicylic acid (SA), lactic acid, and glycolic acid. There are concerns that repeated use of SA and AHAs could cause the dermis and epidermis to be more vulnerable to penetration by UV radiation.

(v) Moisturizers: Moisturizers restore water content to the epidermis and provide a soothing protective film. They improve the appearance and tactile properties of dry and aging skin, restore the normal barrier function of the skin, and reduce the release of inflammatory cytokines. Moisturizers comprise an important therapeutic component in the management of various skin conditions (e.g., eczema, psoriasis, pruritus, and aged skin).

(vi) Topical peptides: These are regarded as cellular messengers that are formed from amino acids and are designed to mimic peptide fragments with endogenous biologic activity. These pentapeptides (e.g., KTTKS) are comprised of a subfragment of type I collagen propeptide and play a role in signaling fibroblasts to produce collagen in the skin, which can improve the appearance of wrinkles.

(vii) Retinoids: They are among the most common ingredients found in cosmeceuticals. In fact, they are the most studied and have the most data behind them. They consist of natural and synthetic derivatives of vitamin A that reduce hyperpigmentation and inhibit enzymes from breaking down collagen.

(viii) Sunscreen: Sunscreens are the single most important cosmeceutical, because they protect skin against solar radiation, which is the most important damaging environmental agent. As a result, they help to prevent the signs of aging. To be effective, sunscreens should provide broad-spectrum coverage that includes both UVA and UVB blocking agents to inhibit photoaging and be part of a daily skin care regimen. Sunscreens contain active ingredients that act as ultraviolet filters.

(ix) Antioxidants: Antioxidants reduce free radical damage, thereby preventing impairment at the cellular level. They inhibit inflammation, which leads to collagen depletion, and they offer protection against photodamage and skin cancer. Common antioxidants include alpha-lipoic acid (ALA), L-ascorbic acid (vitamin C), niacinamide (vitamin B3), *N*-acetyl-glucosamine (NAG), α-tocopherol, and ubiquinone.

Cosmetic Versus Drug

The term cosmetic refers to a preparation designed to enhance the body superficially to hide a real comprehended deficiency or flaw, by direct application. This application is considered to be decorative, lacking in depth or significance, as opposed to a response to a medical requirement. The definition of a drug is more complex. Generally, a drug is a chemical substance which, when absorbed into a living organism, alters normal function. The pharmacology definition of a drug will apply—'a chemical substance used in the treatment, cure, prevention or diagnosis of disease or used to otherwise enhance physical or mental well-being, for a limited duration or indefinite period of time.' Individual governments regulate the availability or drugs to the public as:

(i) Over-the-counter (OTC) medication is available from pharmacies;

(ii) Behind-the-counter medication (BTC) must be dispensed by pharmacist, but does not require the authority of a doctor; and finally

(iii) Prescription-only medicine (POM) can only be prescribed by a licensed medical professional.

There are also numerous bodies that regulate the drugs present in the market including:

(a) The Medicines and Healthcare products Regulatory Agency (MHRA) is a government agency responsible for ensuring that medicines and medical devices work and are acceptably safe. They are responsible for public information as well the investigation and handling of complaints and patient feedback.
(b) The National Biological Standards Board (NBSB) is a non-departmental public body, established in 1975 by Act of Parliament. The board takes responsibility for safeguarding and advancing public health by assuring the following.

Regulations
There is no regulatory category for cosmeceuticals. In fact, FDA does not recognize the word as an official product type, but it regulates cosmetics under the Federal Food, Drug and Cosmetics Act (FDCA). The regulations of cosmeceuticals have not been harmonized between the USA, European, Asian, and other countries yet.

5.4 Proteins, Peptides, and Enzymes as Drugs

Peptides and proteins are complex molecules of naturally occurring 20 different α-amino acid monomers, which joined with each other by peptide bonds. Proteins consist of one or more peptide chains, and peptides are small chains of amino acid monomers and distinguished from proteins by their size (peptide contains <50 monomer units and molecular weight <5 kD, while a protein possesses ≥ 50 amino acids and its molecular weight lies >5 kD). Peptides allow the development of antibodies of a very specific region of a protein, useful for the identification of proteins of interest based on peptide masses and sequence, and peptides are used in clinical research to examine the inhibition of different diseases including cancer. Different fermentation, purification processes, and recombination technology produced potential protein drugs at acceptable cost which can be useful in various diseases through various routes like oral, transdermal, nasal, pulmonary, ocular, buccal, and rectal. Availability and therapeutic application of proteins and peptides as drugs will replace many existing organic-based pharmaceuticals.

Ailments that might be treated with this type of therapeutics include autoimmune diseases, cancer, mental disorder, hypertension, and certain cardiovascular and metabolic diseases. Recombinant technology has allowed the production of many potential protein drugs at an acceptable cost, allowing the treatment of severe, chronic and life-threatening diseases, such as diabetes, rheumatoid arthritis, and hepatitis. The first genetically engineered drug was insulin. The second recombinant enzyme drug was Activase1 (alteplase, recombinant human tissue plasminogen activator). It was approved by the Food and Drug Administration (FDA) for the treatment of heart attacks caused by the blockage of a coronary artery by a clot.

Currently, over 160 protein drugs are available on the world market, and several hundreds more are in clinical trials. The total protein drug market already exceeds 30 billion and is expected to rise by at least 10% a year. One of the biggest opportunity areas in the Protein Therapeutics Market will be in the field of Biogenerics, which is expected to create a multi-billion dollar market in future.

Many protein pharmaceuticals are available for treating rheumatoid arthritis, coronary artery thrombosis, multiple sclerosis, and chronic lymphocytic leukemia (Sheremata et al. 2005; Lequerré et al. 2008; Zhou et al. 2009). Some isolated proteins have been approved by the Food and Drug Administration (FDA) of the USA for clinical use or clinical trials. Some protein pharmaceuticals from Chinese medicine have been developed to treat cardiovascular diseases, genetic diseases, and cancer. Luteinizing hormone—releasing hormone (LHRH) agonist (also called LHRH analog or GnRH antagonist)—is a naturally occurring decapeptide hormone with a molecular weight of 1.182 kD. It is used in the treatment of prostate carcinoma. Insulin is a protein molecule, with a molecular weight of 6 kD. It is used in the treatment of diabetes. Vasopressin is a nonapeptide with a molecular weight of 1.084 kD. It is used as an antidiuretic hormone.

Examples of ten common natural peptides (with the number of their amino acid residues) include: glutathione (a tripeptide) is a common non-ribosomal peptide and a component of the antioxidant defenses of most aerobic organisms, present in most living cells, and stimulates tissue growth; TRH (a tripeptide) is hypothalamic neurohormone and governs release of thyrotropin; angiotensin II (octapeptide) is a pressor agent and acts on the adrenal gland; bradykinin (nonapeptide) is hypotensive vasodilator and acts on smooth muscle; oxytocin (nonapeptide) is uterus-contracting hormone and also stimulates lactation; somatostatin (consisting of 14 amino acid residues) inhibits growth hormone release and used to treat ulcers; endothelin (consisting of 21 amino acid residues) is potent vasoconstrictor and structurally similar to some snake venoms; melittin (consisting of 26 amino acid residues) is honey bee venom and used to treat rheumatism; glucagon (consisting of 29 amino acid residues) is hyperglycemic factor and used as an antidiabetic; and insulin (consisting of 51 amino acid residues) is pancreatic hormone and used in treatment of diabetes.

Bioactive proteins and peptides with various pharmacological properties have been successfully isolated from different Chinese herbs including (i) medicinal fungi such as *Cordyceps militaris*—lectin designated as CML (31 kDa), Ling Zhi-8 (12.4 kDa protein); *Ganoderma* spp.—lectin (a 18-kDa protein); *Poria cocos*—*P. cocos* immunomodulatory protein (35.6 kDa) (PCP); (ii) medicinal plants such as *Viola tricolor*—cyclotides; *Momordica cochinchinensis* seeds—cochinin B (28 kDa ribosome inactivating protein), MCoCC-1 (a 33 amino acid long peptide), chymotrypsin inhibitor designated as MCoCI (7.5 kDa); *Viscum album*—lectin designated as CM-1 (55 kDa) and as ACML-55; the seeds of *Senna obtusifolia*—novel protein (19.7 kDa); *Narcissus tazetta* var. *chinenesis*—*Narcissus tazetta* lectin (26 kDa); *Smilax glabra* rhizomes—smilaxin (30 kDa); *Ginkgo biloba* seeds—ginkbilobin (13 kDa); *Dioscorea batata*—dioscorin (32 kDa); *Trichosanthes kirilowii*—trichosanthin (247 amino acid long peptide); and (iii) medicinal animals

such as *Hirudo* spp. (Leeches)—hirudin; *Eisenia fetida* (earthworm)—earthworm fibrinolytic enzyme—and *Mesobuthus martensii*—antiepilepsy protein (8.3 kDa). These therapeutic proteins, peptides, and enzymes, in vitro and/or in vivo experiments, were found active against different types of cancer, oxidative stress, cholesterol biosynthesis, and some showed antiviral, antibacterial, antifungal, anticoagulant, antiepileptic, anti-HIV as well as immunomodulatory (Byers and Baldwin 1991; Rydel et al. 1991; Wang and Ng 2000; Tsoi et al. 2005; Chu and Ng 2006; Ricotti and Delanty 2006; Chen et al. 2007; Li et al. 2008; Ma et al. 2008; Ooi et al. 2010; Tang et al. 2010).

Important features that distinguish features of enzymes as drugs from all other drugs are (i) their great target binding affinity and specificity and (ii) catalytic properties, and these characteristics have resulted in the development of many enzyme drugs for a wide range of disorders (Vellard 2003). Proteolytic enzymes digest protein by aiding in the digestion process breaking it down into amino acids. They can be taken as a supplement, but better yet, they can be found naturally in certain foods. A great example is papaya, which contains the proteolytic enzyme papain, a popular meat tenderizer. Papain found in papayas may be very helpful for the prevention of atherosclerosis and diabetic heart disease.

Proteolytic enzymes are also known as proteases. The three main proteases are pepsin, trypsin, and chymotrypsin. The protease enzyme breaks down protein found in meats, poultry, fish, nuts, eggs, and cheese and may be helpful for people with food allergies or those who have difficulty digesting protein. Some manufacturers derive their enzymes from animal sources. For example, supplements that contain trypsin or chymotrypsin are extracted from livestock, while supplements that contain papain or bromelain come from plant sources.

Proteolytic enzymes modulate the inflammatory process by a variety of mechanisms, including reducing the swelling of mucous membranes, decreasing capillary permeability, and dissolving blood clot-forming fibrin deposits and micro thrombi. By reducing the viscosity (thickness) of the blood, proteolytic enzymes improve circulation. This consequently increases the supply of oxygen and nutrients to and the transport of harmful waste products away from traumatized tissue. Proteolytic enzymes also help break down plasma proteins and cellular debris at the site of an injury into smaller fragments. This greatly facilitates their passage through the lymphatic system, resulting in more rapid resolution of swelling, with the consequent relief of pain and discomfort in the bones and joints affected. These enzymes can help athletes recover faster from hard workouts and races.

Vellard (2003) mentioned ten FDA-approved enzymes designated as orphan drugs in the USA. They are (i) Adagen (pegademase bovine), for enzyme replacement therapy for ADA in patients with severe combined immunodeficiency disease (SCID); (ii) Ceredase (alglucerase injection), for enzyme replacement therapy in patients with Gaucher's disease type I; (iii) Pulmozyme (dornase alpha), enzyme to reduce mucous viscosity and enable the clearance of airway secretions in patients with cystic fibrosis (CF); (iv) Cerezyme (imiglucerase), for enzyme replacement therapy in patients with types I, II, and III Gaucher's disease; (v) Oncaspar (pegaspargase), enzyme for treatment of acute lymphocytic leukemia;

(vi) Sucraid (sacrosidase), enzyme for treatment of congenital sucrase-isomaltase deficiency; (vii) Elitek (rasburicase), enzyme for treatment of malignancy-associated or chemotherapy-induced hyperuricemia; (viii) Fabrazyme (agalsidase beta), enzyme for treatment of Fabry's disease; (ix) Aldurazyme (laronidase), enzyme for treatment of patients with MPS I; and (x) Replagal (α-galactosidase A), enzyme for long-term enzyme replacement therapy for the treatment of Fabry's disease.

5.5 Pharmacological and Synergistic Activities of Herbal Products

Compared to herbal medicines, conventional drugs are relatively straightforward to investigate because they are of single chemical entities. They can be studied in strict isolation, and there is nothing in the drug's dose form which can interfere to any significant extent with its pharmacological behavior. By the time it reaches the market, the pharmacology of virtually every drug has been exhaustively researched; the physiological response to it can generally be predicted with considerable accuracy and precisely standardized.

Compared to modern medicines of single chemical entities, herbal medicines are very different and usually consist of many compounds, each with separate, varying, and distinct pharmacological activities. From the pharmacological point of view, the situation is unbelievably complex; each component has a different pharmacological activity, but there is invariably an interaction between the different components of the herbal medicine; one component affects other pharmacologically active agents in synergistic way, which means that the effect of combined treatment is more than the sum of each component's individual effects (i.e., certain components in a plant extract can improve the therapeutic effect of active agents). In the patient, one herb can enhance the effect of another given at the same time (i.e., the combined effect of a number of herbal components is actually greater than the sum of each of the individual components). Goldenseal, used for skin infections, contains alkaloid berberine, which in isolation has only weak antibacterial activity. This is potentiated by other substances in the plant, which are inactive themselves. When the herbal ginger extract is used the antiulcer effect is sixty-six times more effective than the active agent, zingiberene, when isolated and used alone, the bioavailability of vitamin C present in many plants is improved when bioflavonoids like rutin are present (Mabey 1988).

The meaning of synergy has now been broadened and extended to include other related concepts. Synergy is now used to describe the effect of one herb in improving the effect of another. For example, use of the laxative senna can lead to stomach cramps in some people. If ginger is taken simultaneously, then these cramps are avoided, or at least minimized. In the practice, herbal medicines are prescribed in a combination of several herbs with the desired outcome of improving

patient benefit. A further meaning of synergy relates to the simultaneous use of herbs with other contributors to health care (combining herbal therapy with adjustment to lifestyle). For example, the herbal therapy for joint pains will be much effective when combined with a specific diet or mild form of exercise. An asthmatic patient will benefit far more when herbal therapy is combined with breathing exercises, chest massage, and improved sleep hygiene.

The mechanism of synergistic effect cannot yet be satisfactorily explained. Based on the nature of the interaction between the components of herbal drugs, two broad types of synergy can be distinguished such as (i) pharmacodynamic interaction (how a drug affects an organism, biochemical, and physiologic effects of drugs on organism) and (ii) pharmacokinetic interaction (how the organism affects the drug or the way in which drugs move through the body during absorption, distribution, metabolism, and excretion of drugs). (i) Pharmacodynamic synergy results from two drugs directed at a similar receptor target or physiological system. For example, combinations of allosteric modifiers at the gamma-aminobutyric acid A (GABAA) receptor create potent synergistic interactions. (ii) Pharmacokinetic synergy results from the processes of drug absorption, distribution, metabolism, or elimination. For example, combined administration of drugs which compete for albumin binding sites on blood cell membrane will elevate the free drug concentrations and thus potentiate their actions (one herbal component may improve absorption and bioavailability of a second). When two psychoactive herbs such as kava and valerian are given to a patient with anxiety, the response is likely to be markedly greater than the sum of the two given separately.

St. John's wort (*Hypericum perforatum*), kava kava (*Piper methysticum*), and valerian (*Valeriana officinalis*) are examples that illustrate synergistic actions (Spinella 2002) and shown in Table 5.13.

Table 5.13 Summary of synergistic mechanisms

Herbal source and contents	Type of synergy	
	Pharmacodynamic	Pharmacokinetic
St. John's Wort contains naphtodianthrones, flavonoids, phloroglucinols, phenolic acids, xanthones, and terpenes	Monoamine reuptake inhibition; MAO inhibition; COMT inhibition	Procyanidin increases bioavailability of hypericin
Kava kava contains kava lactones, principally kavain, dihydrokavain, yangonin, dimethoxyyangonin, methysticin, and dihydromethysticin	GABAA facilitation; Na^+ and Ca^{2+} channel inhibition; MAO inhibition; reuptake inhibition of NE	Kavalactones increase each other's bioavailability
Valerian contains valeranone, dihydrovaltrate, valeric acid, isovaleric acid (monoterpenes and sesquiterpenes)	Multiple GABA mechanisms	Not yet investigated

MAO Monoamine oxidase, *COMT* Catechol-*o*-methyltransferase, *GABAA* Gamma-aminobutyric acid A, *NE* Norepinephrine
[naphtodianthrones (hypericin, protohypericin, pseudohypericin, and protopseudohypericin)]

The above table illustrates multiple examples of pharmacodynamic and pharmacokinetic synergy at work in psychoactive herbal medicines. St. John's wort shows evidence of pharmacodynamic synergy through monoamine neurotransmitter systems, preventing neurotransmitter breakdown and blocking reuptake. Pharmacokinetic synergy is evident in St. John's wort since procyanidin (flavonoids) increases the bioavailability of the naphtodianthrones (hypericin). Kava kava's effects on GABA and voltage-gated ion channels (and possible monoamine systems) create pharmacodynamic synergy. Kava kava also shows evidence of pharmacokinetic synergy since the administration of combined kava lactones increases brain bioavailability of each, compared to individual administration. Valerian shows evidence of pharmacodynamic synergy since multiple constituents of the herb are acting on GABAergic systems, both pre- and post-synaptically. Pharmacokinetic synergy in valerian is possible, but has not yet been investigated.

The above examples of synergy are directly relevant to the therapeutic benefits of these herbal medicines. The synergistic effects of St. John's wort likely enhance its effects on monoamine neurotransmitter systems, the predominant mechanism of most antidepressant drugs. The synergistic interactions of kava kava occur through GABA, voltage-gated ion channel, and monoamine systems. All of these mechanisms help account for kava kava's demonstrated antianxiety effects. The synergistic effects of valerian's constituents on GABA transmission would explain its demonstrated effects on sleep.

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